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# THE MONTREAL GENERAL HOSPITAL SPECIAL ISSUE

## FOREWORD

### The Montreal General Hospital Special Issue

The present issue of the Journal commemorates the completion of the new buildings of the Montreal General Hospital. The hospital was founded in 1819, and its first building erected in 1822. From then on its growth and work reflect in many respects the history of a rapidly growing city. As the only English hospital in Montreal till late in the century, it carried on a great volume of work, taking part not only in the dramatic epidemics of the period but also in the still more significant changes which have occurred in the medical and hospital world in the last hundred years and more.

Eventually, in spite of constant enlargement of the hospital, the original site became unsuitable for the physical expansion needed in an active institution. But even so, the decision to move away and rebuild was made only after prolonged consideration of the many factors involved. The planning, raising of funds and construction occupied a period of more than eight years, the actual building operations requiring three years; the new premises were finally occupied in May 1955. Her Royal Highness the Princess Royal graciously consented to open the buildings formally in October, during her visit to Canada.

Striking as the new buildings are in their attractive site and with their modern equipment, they still are no more than a fresh stage in the long life of the hospital. Its real pride lies in maintaining its age-long tradition of service, especially to the sick poor. The original staff, all Edinburgh trained, insisted from the beginning on giving clinical instruction in the hospital, and teaching has been carried on in its wards uninterruptedly since 1824. The later incorporation of their private medical school (the Montreal Medical Institution) as the Medical Faculty of McGill University (1828) resulted in the mutual strengthening of two great institutions.

With its unusual opportunities the hospital has attracted to its staff many whose names shine brightly in Canadian medical history: its original founders, Robertson, Caldwell, Holmes and Stevenson; Palmer Howard and his famous protégé, William Osler; George Fenwick; F. J. Shepherd; Thomas Roddick; H. A. Lafleur; F. G. Finley; and A. H. Gordon, to name only a few. Their present-day successors show in this issue that they have maintained in full degree the hospital tradition both of caring for the patients and of extracting from the great variety of material all that adds to our knowledge of disease and its treatment.

H. E. MacDermot

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### The Functions of a Hospital

When Henry VIII of England established St. Bartholomew's Hospital on a new basis as a hospital for the sick poor he was "moved thereto with great pity for and towards the relief and succour and help of the poor, aged, sick, lame and impotent people". When it was proposed to found the Edinburgh Royal Infirmary, the institution in whose wards the first medical staff to the Montreal General Hospital were later trained, the pamphlet circulated states that "humanity and compassion naturally prompt us to relieve our fellow creatures when in such deplorable circumstances as many are reduced to", and mentions the second function of a hospital, "that students in physic and surgery might

have a better and easier opportunity of experience". In contrast to this, a zealous authority on hospitals recently listed the functions of a hospital, in the following order, as (1) research; (2) physician and nurse training; (3) patient care.

Does this curious inversion of functions listed in the last sentence really represent a general, or even a desirable, change in thinking on the subject since Henry VIII's time? Should the care of the patient come last on the list, on the plausible argument that the fruits of research convey a greater overall benefit to mankind? The Montreal General Hospital would certainly not agree with this shift in emphasis. Its tradition of service to the sick will undoubtedly take pride of place in the new building, without in any way jeopardizing teaching or research. We do not pay special tribute to the Montreal General Hospital because of its age, or because of its great reputation in the training of physicians and nurses, or because of the many excellent pieces of research begun within its walls. We pay tribute to it principally because it has never lost sight of the fact that its most important function is to give to the sick, medical care of the highest quality. In doing this it has also striven for an ideal aptly expressed by the first Board of the National Hospital, Queen Square, London, "to afford the poor inmates in times of sickness not only the best medical care but, what is equally important, a happy dwelling and cheerful associations". May the new Montreal General Hospital long continue as a happy dwelling with cheerful associations!

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## VIRUS REPRODUCTION AND VIRUS DISEASE*

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THE MECHANISTIC ERA in virus diseases of man was opened in 1902 by Reed and Carroll.[1] They and their associates recorded a number of remarkably precise observations on the etiology of yellow fever that have since been abundantly confirmed (*cf.* Theiler[2]). Some of their findings bear directly on ideas which are developed in this communication. Thus, in their now classic studies with human volunteers, which proved the correctness of the theory that yellow fever was transmitted by the bite of an Aëdes mosquito, they made the following observations. Mosquitos became infective when they had taken a blood meal during the first three days of the disease. Mosquitos did not become infective when they bit early in the incubation period or late in the disease. Mosquitos were not infective soon after they had bitten and became so only after a period of 12 days or more. They then remained infective for life. These findings, so puzzling at the time, are now fully understood (*cf.* Strode[3]). Each can be explained on the basis of modern knowledge of virus reproduction and the results thereof.

Yellow fever is still one of the most classic of the virus diseases of man, and it may be rewarding to review its pathogenesis briefly. When an infected mosquito bites, a very small amount of yellow fever virus is introduced into the blood. This small amount of virus then promptly disappears. The virus does not reappear in the peripheral blood until just before the disease develops. Therefore, normal mosquitos biting during the four-day incubation period do not take in virus. However, during the incubation period, the virus is undergoing reproduction in cells of the liver and other organs. When the number of cells damaged by the reproductive process becomes large enough, symptoms and signs of yellow fever rapidly appear. At about this time large numbers of newly formed virus particles are released from the infected tissues into the blood. Now if a mosquito bites, it will take in virus.

As the disease progresses, still higher concentrations of virus develop in the liver, lymph nodes, and kidneys. This is the result of continued virus reproduction. In parallel, the concentration of virus in the blood increases rapidly and may reach a level of $10^7$ particles per ml. If a mosquito bites at this time, it will take in a considerable amount of virus. After about the

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fourth day of disease, neutralizing antibodies begin to appear, and as they increase in concentration, the number of infective virus particles in the blood rapidly decreases, and finally such particles disappear. Thus, late in the disease a biting mosquito fails to take in any infective virus and so cannot transmit the agent.

Analogous events occur in the mosquito itself. After ingestion of infective blood, the virus is first carried to the stomach of the insect and then is distributed to other organs. Only after the virus has reproduced in numerous cells in the insect does it eventually reach the salivary glands. This process takes about 12 days, and during the period the mosquito, although actively supporting virus reproduction, is not mechanically able to transmit the agent. The mosquito does not develop neutralizing antibodies and, being unable to rid itself of the virus, remains infective for life. Despite extensive virus reproduction, tissue damage apparently is not produced, and therefore disease does not develop in the mosquito.

Although the details of pathogenesis have been documented more thoroughly for yellow fever than for any other virus disease of man, there is now sufficient information about a number of such infections to support a general conceptual scheme: only a very small number of infective virus particles are needed to initiate virus reproduction in a person who has had no previous contact with the agent. On theoretical grounds, a single particle should, if it is adsorbed by a susceptible cell, initiate reproduction. This has, in fact, been demonstrated with vaccinia[4] and influenza viruses[5] in experimental animals. Each new virus particle from a cell can initiate reproduction in another susceptible cell. Thus, if a cell yields 100 new particles, 100 other cells of similar type can be infected and will produce a similar yield. This appears to be the basis for the logarithmic increase in virus concentration which is the regular result of reproduction.

The duration of the incubation period seems to be dependent upon two independent variables: the number of cells initially infected and the rate of virus reproduction. The larger the number of cells initially infected, the shorter is the incubation period. The rate of virus reproduction appears to be directly related to the duration of the incubation period; the slower the rate, the longer the period. Experiments with influenza[6] and other viruses[7] in animals have demonstrated that when both variables are known the incubation period can be predicted with considerable precision.

Virus disease develops only if virus reproduction occurs, but reproduction can occur without leading to disease. As a result of reproduction, the concentration of virus particles increases in infected tissue at a logarithmic rate and reaches a high level before either signs or symptoms of infection appear. This has been found to occur in every instance so far studied. The severity of the disease may be largely determined by the concentration of virus particles in the infected tissues. Experiments have demonstrated a direct relation between virus concentration and extent of lesions with a number of viruses in animals.[6, 7] From this it can be deduced that the extent of the lesions is dependent on the number of cells damaged by the reproductive process or its products.

Recovery occurs when the rate of the virus reproduction decreases. The most probable means is through reduction in the number of susceptible cells. Because recovery sometimes coincides with the appearance of antibodies against the virus, it has been held that the development of specific antibodies is responsible for recovery. There is strong evidence against this view, e.g., recovery from recurrent herpes simplex occurs without a change in antibody level, recovery from psittacosis is not associated with the appearance of significant amounts of neutralizing antibody, and the injection of immune serum does not definitely lead to recovery in any virus disease.[8]

Persistent immunity, which is of common but not uniform occurrence, is best explained by the persistence of the virus. Evidence for persistence has been obtained in a number of instances.[8] The theory of virus persistence requires that continued reproduction occur even though this be at a very slow rate. However, it is not necessary to assume continued presence of virus in all susceptible cells to explain persistent immunity. The antigenic stimulus provided by a small amount of slowly reproducing virus would maintain antibody production, and neutralizing antibodies are highly effective in preventing a second infection in the large majority of instances. In the case of transient immunity, as with influenza and certain other com-

mon respiratory infeetions, the virus may in fact be eliminated, for these are typically surface cell infections.

Although virus disease does not develop in the absence of virus reproduction, it is not a regular or even the most common sequel of the reproductive process. Virus disease is attributable to damage of cells, and the development of damage depends on the nature of the virus, its rate of reproduction, and the concentration reached as well as upon the nature of the cell itself. Alteration of any one of these variables may yield a system in which reproduction occurs but disease does not develop. The easiest variable to alter is, of course, the type of cell infected. Thus, reproduction of mumps virus in the human parotid gland or meninges leads to obvious disease. Yet the same virus on comparable reproduction in the chicken embryo causes no damage.[9] Similarly, the reproduction of influenza viruses in the upper respiratory tract of man or the ferret often induces disease, but does not in the mouse until so-called adaptation has occurred.[10] The effect of the rate and extent of reproduction is evident from studies with virus variants. So-called avirulent or attenuated viruses, which do not induce obvious disease, reproduce at a slower rate and yield lower concentrations of virus than virulent strains of the same agent.[11, 12]

Direct evidence that virus reproduction is an essential prerequisite for the development of virus disease is secured when the reproductive process is inhibited by suitable compounds. As an example, certain bacterial polysaccharides inhibit the reproduction of some small viruses in experimental animals and thereby prevent the development of disease.[13]

It seems clear now that the crucial problem in virus disease is, in fact, virus reproduction. If the mechanism of virus reproduction can be worked out and the process controlled, means for the management of virus diseases may be at hand. The important questions are: How do viruses multiply inside living cells, and how does this process sometimes damage the cells? What are the biochemical events necessary for synthesis of new virus particles, and how do they alter cell metabolism?

## REPRODUCTION OF BACTERIAL VIRUSES

Some startling answers to these questions have emerged from recent studies on bacterial viruses (*cf.* Hershey and Bronfenbrenner[14]). There is now a comprehensive scheme to explain the reproduction of these agents. It may be of value to review this in brief and then to determine how it fits in with present information on the reproduction of viruses that infect man.

Bacteriophage particles resemble tiny sperm and have both a head and a tail-like structure.[15] The shell of the head and the tail are composed largely of protein. Inside the head there is nucleic acid, and this is entirely of the desoxyribose type. A single phage particle can infect a bacterium. Only the tail penetrates the bacterial wall, and nucleic acid from the head is introduced. The phage particle itself does not enter the bacterium. In fact, the head-shell and part of the tail can be removed at this stage, and yet phage reproduction will still occur in the bacterium.[16] This phenomenon appears to be unique in biology. The phage particle, in the process of initiating reproduction, disintegrates, and its chief contribution to the bacterium is nucleic acid. Shortly after this there are surprising developments (*cf.* Luria[17]). The bacterium stops synthesizing bacterial components and begins to produce phage nucleic acid and phage protein.[18] The two are made separately, not as intact phage particles. After a time tailless heads appear in the bacterial cytoplasm.[19] Later the final assembly of the phage particle is achieved by the addition of the tail and the introduction of nucleic acid.

The new particle is now infective. The bacterial cell which supported this process is so damaged that it disintegrates and releases more than 100 new phage particles. Each new particle can initiate this complex reproductive cycle as soon as it finds another suitable uninfected bacterium. Thus, with phage, reproduction is dependent on a series of discrete biosynthetic processes which produce the required precursor materials separately and finally put them together as new phage particles (*cf.* Lwoff[20]). In supporting this remarkable process, the bacterium is driven to commit suicide.

If this concept is valid, it should be possible to control phage reproduction by inhibiting the production of any one of the required precursor materials or by preventing the final assembly of mature phage particles. Such control has, in fact, been accomplished. Chloramphenicol and analogues of tryptophane inhibit protein syn-

thesis in bacteria. As would be expected, they prevent phage reproduction when applied during the stage of phage protein formation.[21, 22] Certain pyrimidine analogues may inhibit nucleic acid synthesis in bacteria, and some inhibit phage reproduction when applied early in the process.[23] Proflavine does not prevent the synthesis of either phage protein or nucleic acid but does prevent final assembly of the mature particle.[24] Only tailless heads are produced when this compound is applied late in the reproductive cycle, and these are not infective. Apparently, however, the damage to the bacterium occurs while phage protein and nucleic acid are being formed, and proflavine, although preventing assembly of the particle, does not protect the bacterial cell from destruction. It disintegrates at the expected time but does not yield infective phage particles.[25]

### COMPARISON WITH ANIMAL VIRUSES

One may now ask, in what respects does the reproduction of animal viruses correspond with the reproduction of bacterial viruses? It appears that there may be some differences, but their importance is not yet clear. Viruses which infect man resemble tiny spheres (*cf.* Stanley and Lauffer[26]). No tail-like structures have been positively identified. They are composed largely of protein and nucleic acid, like phage particles, but some contain the ribose type, others the desoxyribose type, and certain may contain both. Some have central dense areas resembling tiny nuclei.[27] One virus particle can often initiate reproduction in a susceptible cell, but precisely how this is accomplished is not yet known. If the intact particle actually enters the cell, some change occurs, for it cannot be recovered later.[28] Whether or not the particle actually disintegrates, as does phage, is not yet clear. There then occurs an eclipse period during which there is no direct evidence as to intracellular developments. Some indirect evidence supports the idea that required precursor materials are formed during this period, as with phage, but their demonstration has not yet been achieved. Later, formed elements resembling virus particles begin to appear in the cytoplasm, and then they increase in number. Recent evidence suggests that some viruses may develop limiting membranes before release from the cell.[27] Unlike phage, the reproduction of many animal viruses does not lead to destruction of the cell. Presumably, the biochemical alterations produced in the cell are often not as severe as those caused by phage reproduction. The number of new particles produced varies from a few to more than 1,000 per cell, depending on the virus.[29] As with phage, each new particle after release can initiate another reproductive cycle when it finds another susceptible cell.

So far there are no data that make the phage scheme clearly inapplicable to the reproduction of animal viruses. If the process is like that of phage, dependent on the production of precursor materials during the eclipse period, it would be expected that reproduction should be inhibited by substances analogous to those that inhibit phage reproduction. There is evidence in support of this idea. Thus, certain amino acid analogues, such as methoxinine or ethionine, may inhibit protein synthesis in cells. When applied early in the eclipse period, they can inhibit influenza[30] and poliomyelitis virus reproduction.[31] Moreover, some pyrimidine or purine analogues, such as 2,6 diaminopurine, may inhibit nucleic acid synthesis in cells. Early in the eclipse period they can inhibit the reproduction of vaccinia[32] and encephalitis viruses.[33] Acridine compounds closely related to proflavine, which prevents assembly of mature phage particles, can inhibit the reproduction of influenza and mumps virus.[34] Finally, certain glycosides of benzimidazole inhibit the reproduction of influenza viruses only when they are applied during the first half of the eclipse period.[35] This is well before any new infective particles have appeared. In addition, unlike most other inhibitory compounds, some glycosides of benzimidazole do not cause demonstrable cell damage even though they are highly active as inhibitors of influenza and mumps virus reproduction.[36]

### INHIBITION OF VIRUS REPRODUCTION

Thus, it appears that even as judged from the effects of chemical inhibitors of reproduction, the available evidence does not require the construction of a scheme for animal virus reproduction different from that for phage reproduction. Because virus disease is dependent on virus reproduction and since reproduction can be inhibited by chemical compounds, it might be held that effective chemotherapy awaits only the finding of less toxic and more potent compounds. This idea seems sufficiently logical and so well

supported by experimental evidence that an obvious difficulty may be overlooked. This difficulty was implicit even as early as 1902 in the work of Reed and Carroll[1] on yellow fever. It will be recalled that mosquitos became infective when they bit patients on the very first day of yellow fever. This was because a large amount of virus was already present in the blood. The virus had reached the blood only after extensive reproduction in the liver and other organs. This process occurred during the incubation period. Comparable findings have been obtained consistently when human volunteers were inoculated with various viruses. Much virus reproduction occurs before the signs and symptoms of disease develop, and on the last day of the incubation period the concentration of virus in the infected tissue is usually high, often as high as during the full-blown disease. Experiments in animals with a variety of viruses have served merely to affirm and considerably to extend this general principle.

Therefore, it appears that although inhibition of virus reproduction is a potentially feasible means for controlling virus diseases, it may need to be accomplished before the disease is full-blown if it is to be effective. To be most effective, it may prove to be necessary to inhibit virus reproduction during the incubation period.


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## RÉSUMÉ

Les travaux de Reed et Carroll sur l'étiologie et la pathogénèse de la fièvre jaune sont devenus l'un des classiques de la virologie et plusieurs de leurs observations servent encore de base aux recherches dans ce champ d'activité. Une quantité infime de virus est introduite dans l'organisme après la piqûre d'un aèdes. Ce virus disparaît sans laisser de trace. Pendant la période de quatre jours qui constitue l'incubation, il se multiplie dans les cellules du foie et des autres organes. Ce n'est que lorsqu'un nombre suffisant de cellules deviennent infectées que les manifestations cliniques apparaissent. Le virus peut alors être trouvé en quantité considérable dans le sang. Dès l'apparence des anticorps, cette concentration tend à diminuer et finit par disparaître complètement. Les mêmes phases se retrouvent chez le moustique, sauf que l'insecte ne peut produire d'anticorps. Théoriquement, une seule particule de virus peut causer la maladie, et chaque particule d'une cellule infectée peut infecter autant d'autres cellules, ce qui expliquerait la progression logarithmique de leur reproduction. L'incubation dépend du nombre de cellules infectées d'emblée et de la vitesse de reproduction du virus. Les maladies virus se manifestent seulement s'il y a reproduction du virus, mais par contre la reproduction peut se produire sans la maladie. La cellule bactérienne subit une telle détérioration qu'elle se désintègre et libère au-delà de cent des nouvelles particules de bactériophages auxquelles elle vient de donner naissance. La reproduction du bactériophage pourrait être enrayée en empêchant la synthèse de la protéine (c'est ce qu'accomplissent le chloramphénicol et les analogues du tryptophane, ainsi que d'autres analogues de la pyrimidine), ou l'assemblage final des têtes et des queues (comme le fait la proflavine, produisant ainsi une quantité de têtes sans queues).

Les virus qui infectent l'organisme humain ressemblent à de petites sphères sans queue. Le mode exact de leur reproduction intra-cellulaire est encore inconnu. Plusieurs types de virus peuvent se reproduire sans causer la destruction de la cellule. Le nombre des nouvelles particules produites varie de quelques-unes à plus d'un millier par cellule. Si la reproduction dépend de la fabrication de matériaux précurseurs, on pourrait s'attendre comme chez le bactériophage à sa suppression par la présence de substances analogues à celles qui empêchent la reproduction du bactériophage. Ainsi, la méthoximine ou l'éthionine peuvent maîtriser la reproduction des virus de l'influenza et de la poliomyélite. Certains dérivés des purines peuvent interrompre la reproduction des virus de la vaccine et de l'encéphalite. Il semble que la chimiothérapie n'attende que la découverte de composés moins toxiques et plus puissants. L'intervention la plus efficace devrait probablement se faire pendant la période d'incubation. M.R.D.

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# MEDICAL EDUCATION IN EUROPE AND NORTH AMERICA
## (SOME COMPARISONS)

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IN OFFERING some brief remarks comparing systems of education in faculties of medicine in Europe and North America, it is obvious that the writer is both incautious and presumptuous, since one must have adequate knowledge of the background of various systems and the cultural situation in which they have developed. It is, therefore, with some hesitation that such a title is used, as a means of presenting some suggestions for alteration of the pattern of medical education in North America; the writer is aware that such comparative statements are possibly based on faulty observation and interpretation, and on too brief an enquiry. Any comparisons made are not intended to be hypercritical or derogatory, and are entirely the personal responsibility of the author.

Among the obvious problems in medical education, both in Europe and North America, there are four which preoccupy teachers in medical schools in both areas; for purposes of comparison it is proposed to comment on these, in the light of current practices. These problems are: (1) methods of student selection, (2) methods of teacher selection and training, (3) graduate training, and (4) the medical curriculum.

### STUDENT SELECTION

Student selection procedures, as they are commonly practised in North America, are almost unknown in Continental Europe. In any country where the university educational system is part of the State Ministry of Education, with responsibility for support of the university from funds provided by the taxpayer, no student may be refused admission to the university if he is able to qualify on academic grounds; this means that assessment of personality, of emotional maturity, or of motivation, plays no part in the admission procedures in Continental schools, but only the academic record; in North America all these factors do play some part in the selection of the student for admission to a faculty of medicine, but as yet too much importance is given to the item of academic rating and ability to secure good grades in examinations. As a result of the lack of selection procedures in Europe, the selection of potential doctors becomes a continuing process throughout the course of medical instruction, since by failing the unworthy student in examinations the size of otherwise unwieldy classes is kept within reasonable bounds. As an instance, the faculty of medicine of the University of Paris may admit some 1,500 or 1,600 students to the first year but, because of the strenuous examinations, at the end of some six years of study only about one-fourth of this number will actually graduate, the remainder having been failed in their examinations during the five-year course. Such a method is time-consuming and wasteful both for the student and for the teacher.

In selecting students for admission to medical schools in America, something more than lip-service is given in most faculties to the necessity of a broad educational background for the potential doctor; unfortunately, too much weight is still given to the student's credentials which attest to his education in the so-called "scientific" fields of chemistry, physics and biology, instead of insisting on a broad and mature education in fields relating to the humane and social sciences.

Most European schools do not at the end of a period of undergraduate education in a medical faculty grant the doctorate degree; rather, a practitioner's licence or a bachelor's degree is granted at the end of the undergraduate period. The doctorate is granted usually after a further year of study in the medical school and the presentation of a thesis. Particularly in Scandinavian countries, the possession of a doctorate in medicine is regarded as the mark of a well-educated physician or surgeon, in that during the year or two of further study which is required, the student not only gains a knowledge of the current literature, but has also probably done some independent scientific study, and has acquired the habit of organizing his knowledge in a manner fit for presentation to others, and facility in observation of factual material and its presentation. Such a procedure has much to recommend it.

### TEACHER SELECTION

It is the constant and recurring wonder of teachers in faculties of medicine in Europe that medical schools in America are able to provide such a high teacher-pupil ratio during the medi-

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cal course. Commonly, in Continental Europe part-time teachers are little used, and the didactic method of instruction rather than the group method is still in vogue, in which the professor in a given discipline carries almost alone the full burden of the teaching of his subject. This means that the teacher-pupil relationship is rarely as warm or friendly as in schools in North America. In Continental Europe the professor gives his daily lecture which the students attempt to note verbatim, in preparation for the examination which may be set by the same professor. His scientific assistants, particularly in the basic sciences, may have little or no contact with students, being engaged primarily in fields of research, which may approximate closely the field in which the professor himself has made his own reputation.

While it is possibly true, though I personally doubt it, that "teachers are born, not made", it would seem reasonable to suppose that few potential teachers, having adequate knowledge and interest, would not be bettered in their teaching performance if they could be provided with some pedagogic training, particularly in the fields of the arrangement of material, elocution and method of presentation. Few teachers are without some aspects of an "enquiring mind," but many having this turn of mind are indifferent teachers, because of lack of self-confidence and facility in the use of their mother tongue. Such lacks could, it is suggested, be readily overcome by even a short course of training in modern pedagogical methods. Of course, the striking difference between the teacher-pupil ratio in Europe and America is essentially a problem of the economic support which is given to the medical school; and while we in North America are all too conscious of our lack of adequate salary for assistants, we are, in the writer's opinion, doing a fairly adequate job with the means at our disposal, in providing to the student such a large number of competent teachers and demonstrators.

### GRADUATE TRAINING

There is nowhere yet in Continental Europe any system of graduate training comparable to the residency system of the American Continent. The graduate in Europe may attach himself, with the professor's permission, to the laboratory or clinical wards, but usually during his first two or three years he has relatively little status, responsibility or authority, and is a purely "voluntary assistant," being permitted to aid in various laboratory or clinical procedures. He is not, however, under the more strict discipline of the junior-senior intern residency programme as found in our schools, nor is he under the constant supervision of his seniors by being permanently resident in the hospital during his clinical training, but lives outside the hospital walls. So-called "refresher" courses and lectures are now being provided in some areas in Europe for men who are in practice, but other than this and the annual meeting of national or provincial medical societies, little progress has been made in providing "continuing" education such as is carried out in North America by means of longer or shorter refresher courses, the sending of teams of lecturers to local medical groups, or the provision, as in some areas of the United States, of the services of a teaching resident from a university hospital, for a period of a month, to a smaller non-teaching hospital.

### THE CURRICULUM

Any discussion of the curriculum in a medical school will, of course, raise the usual questions:

(a) What are we educating the student for—a family doctor, a research student, a teacher?

(b) What constitutes success in medicine—the finding of new knowledge, financial success in practice, or medical administration or other forms?

(c) What is the relationship of the doctor to the social community; and his responsibility thereto as one of the "educated" persons in that group? An estimate of his future function should bear relationship to his training.

Until some definitions are given as to what we are educating the student for, it is perhaps unrealistic to decide on any *firm* curriculum which may be suitable in 1955 and unsuitable in 1965. This is one of the difficulties of the European curriculum; since it is fixed in most instances by parliamentary legislation or ministerial regulation, latitude for change is extremely confined. However, the curriculum structure in our schools in North America is equally at fault, in that we have not yet been able so to arrange our schedules that adequate opportunity is given for the presentation of aspects of family practice, which are likely to be of more benefit to the community than the relatively decreasing

importance of morphology with which we now crowd the student's mind, instead of giving him more opportunity to learn of the peculiarities of human nature, and the various reactions of his mental and social environment on the patient's bodily health. It would seem that some sacrifice of teaching of morphology must be made in favour of the teaching of the humanities and the social sciences, or even comparative religion: I can think of no better background for the study of group prejudices related to medical care in a community than some knowledge of comparative religion and ethics.

I would decry our present preoccupation, in both medical education and medical care, with the episodic aspects of illness, rather than concern with the direction of our teaching and our therapy toward the whole patient as a social being and the environmental, social or emotional implications of his illness. This suggestion must refer back to the quality of medical teaching and to the truly educational aspects of our preparation for a life in medicine, and even to the selection of students for admission—equally to the selection and training of teachers in medical schools. I would suggest that the method of selection of students—potential doctors—should be based as much, if not more, on assessment of character, admittedly difficult and liable to errors of judgment, as on proven academic ability as shown by performance in examination, and on the possession by the candidate of that indefinable attribute called "human compassion," without which the study and the practice of medicine is a dreary, unattractive chore. Too many of our admission practices ignore the need for these human traits.

I would not suggest that curricular change is the only, or necessarily the greatest, variable needed in our educational process: there are several other important factors. Some were recently enunciated by Dr. Ward Darley[1] in his presidential address to the American Association of Medical Colleges: namely, the inherent capacity of the student; the strength of his motivation in the study of medicine; the number and severity of his distractions and anxieties, whether financial, marital or military; the ability and strength of leadership provided by the faculty; the suitability of the teaching equipment in laboratories, and the availability of clinical teachers and patients. The sum of the interplay of all these factors is what we call medical education. However, I do feel that one variable to which scant attention is given is the student and his capacity and opportunity to learn, and his need for a personal relationship with some member of the teaching staff who may act as a friendly adviser or counsellor. Too much of our teaching effort is devoted to moulding all students into the same pattern, requiring them to provide the same type of answers to examinations, and to do the same work with equal skills, which is obviously impossible since all are not equally gifted; in sum, too much teaching and not enough learning.

For a full and satisfying life, the doctor, as a student, must have his mind turned to continuing his professional education throughout his whole career, but also, as a responsible member of an organized political society, he must have some common ground of knowledge and scholarship through which he can communicate with the general public outside his own professional group. Hence, undergraduate medical education must be broad, in the sense of including study in the fields of the social sciences and the humanities, even though I am aware that our current educational practices already open more doors of opportunity into various walks of life than almost any other, but it is probably a fair assumption that the place of medicine in society will be different in 1975 from what it is now. Until that place is decided, obviously it is impossible to train medical personnel for all the eventualities, but I do feel that some forward looking is necessary, and I would suggest that some of our teaching, both as to method and context, must be altered if we are to prepare not only better technicians but also better doctors for the service of society. For, truly, we are the servants of the community, whether we serve as family physicians, specialist surgeons, academic teachers, editors of medical journals, or administrative officers.

Society has not, recently, been too well satisfied with our services; hence changes are occurring in the forms of service, and of payment for medical care and, rightly or wrongly, society is likely to receive the type of care it desires. I am sure that a more broadly trained physician—broad in the sense of ability to think with, and communicate to, the community—will have a greater influence on community medical care

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than one with a narrower point of view. The chief purpose of a teacher in a medical school is to arouse curiosity in the student. Only those teachers who are naturally curious, and who follow this curiosity into the laboratory of a medical practice or a medical school, are able to arouse the curiosity of the student and to aid in the development of an enquiring mind.

The following quotation is from a recent report by Severinghaus *et al.* on "Preparation for Medical Education in the Liberal Arts College":[2]

> Up to the present there is little evidence that medical schools stress "maturity" as a more significant criterion for admission; similarly, there is no evidence that medical schools are planning to provide liberal education for their students: the ideas of combining medical training and liberal education can be dismissed as being unwise or impracticable, but not as being impossible.

This prompts me to suggest that not only is a combination of liberal education possible with a medical-technical training, but it has become essential. From the time the potential doctor enters college until he has completed two years of intern training in a hospital, he has been under university guidance for a period of *ten years*, which includes tuition and laboratory and study of at least ten thousand hours, and has promoted the expenditure of his own or public moneys to the sum of $25,000! Yet we have not laid down any complete plans for this educational experience, excepting in periods of two or four years, and such periods, in spite of our efforts of integration, frequently bear little or no relation one to another.

It is the writer's thesis that we, as teachers, must look at the whole field of ten years as a single educational experience, and so arrange our curricula that more than a smattering of science, and an equally more thorough study of the humanities or social sciences, is provided during this period. Surely it is within our competence so to co-ordinate the instruction which is now miscalled "pre-medical" with that which is now called "medical education," but is essentially a training in a technique, that at the end of the ten-year period a mature and truly educated physician, having not only adequate technical competence, but also a knowledge of the æsthetic and political aspects of life, will be the product of our schools, which we are prepared to offer to the community with our blessing, confident that the reputation of our profession is in worthy hands.

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## RÉSUMÉ

L'auteur nous prévient que toute comparaison entre les systèmes de formation médicale européen et nord-américain est assez difficile. Il réclame la responsabilité de ses opinions.

En Europe comme en Amérique, la formation médicale présente surtout quatre problèmes: (1) le choix des étudiants; (2) le choix et la formation des professeurs; (3) l'entraînement des jeunes médecins; (4) le programme des études.

1. Dans les universités d'Etat, comme à l'Université de Paris, on ne refuse aucun étudiant présentant les qualifications scientifiques requises; on ne se préoccupe ni de sa personnalité, ni de la maturité de son caractère; l'élimination se fait par le moyen d'examens extrêmement ardus pendant la durée du cours. Cette méthode entraîne une grave perte de temps pour l'étudiant et pour le professeur. En Amérique, tout en réclamant une bonne culture générale, on se préoccupe encore trop des points obtenus en physique, chimie et biologie, et pas suffisamment de l'humanisme et des sciences sociales. Presque toutes les universités européennes n'accordent le doctorat qu'après un an d'études supplémentaires et soutenance d'une thèse. Ainsi, le titre de docteur en médecine représente, surtout en Scandinavie, une distinction particulière révélant un esprit plus mûr, un jugement mieux exercé, l'habitude de l'observation et la facilité d'exposer ses opinions.

2. Les Européens sont toujours surpris du grand nombre de professeurs par rapport au nombre des étudiants dans les universités américaines. En Europe, un seul professeur peut être chargé d'une nombreuse classe; il n'a pas le temps de connaître ses élèves personnellement. Les professeurs gagneraient à suivre un cours de pédagogie, surtout en ce qui regarde l'élocution et la division et la présentation de la matière à enseigner.

3. On ne trouve nulle part en Europe un système d'entraînement des jeunes médecins comparable à notre système d'internat et de résidence en Amérique. Dans quelques régions européennes, on donne maintenant certains cours de revision pour les practiciens. En somme, peu de progrès dans l'instruction post-universitaire. En Amérique, nous bénéficions de cours de revision et de leçons données aux médecins éloignés par des groupes de professeurs ou d'un professeur résident envoyés spécialement à cet effet.

4. Le programme des études pose divers problèmes, à savoir: (a) que deviendra le futur médecin: un médecin de famille, un homme de laboratoire, ou un professeur? (b) qu'est-ce qui représente la réussite pour un médecin: une découverte scientifique, la fortune, la bonne administration, etc.? (c) quelle position le médecin occupera-t-il dans la société? quelle sera sa responsibilité comme membre d'une élite? Le futur médecin devrait étudier davantage les humanités, les sciences sociales et même les différentes religions. Cette dernière connaissance surtout l'aidera grandement à comprendre beaucoup des préjugés de ses clients. Le futur médecin devra s'habituer à considérer son patient, non comme un cas, mais comme un être social placé dans un certain milieu dont il faut tenir compte, avec une grande sympathie.

L'étudiant devrait pouvoir se confier et demander conseil à l'un quelconque de ses professeurs. L'auteur insiste sur l'importance d'une culture générale étendue et sur cet attribut qu'on nomme: la maturité d'esprit. Les études médicales et pré-médicales devraient former, non pas seulement des techniciens, mais des médecins au jugement mûri, bien instruits des différents aspects esthétiques et politiques de la société et de la vie.

M.R.D.

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# STAPHYLOCOCCAL EMPYEMA*

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DURING THE PAST YEAR 17 cases of pneumonia in infants and children, all due to a penicillin-resistant staphylococcus, have been identified on the pædiatric and surgical services of the St. John's General and St. Clare's Mercy Hospitals. Every one of these cases presented radiological or post-mortem evidence of lung abscess; 12 cases had, in addition, a bronchopleural fistula with tension pneumothorax and empyema.

In this series of 17 patients, 15 ranged in age from two to 21 months. One patient was six years of age and one was a 15-year-old boy. In nearly every case the pneumonia occurred either during hospitalization for some other illness or after a recent period of hospitalization or residence in a children's home.

Clinically, all cases presented a typical picture of pneumonia with cough, cyanosis, rapid respirations, high temperature and obvious clinical signs on physical examination. The white cell count was elevated, counts up to 50,000 being recorded. On penicillin therapy there was a dramatic lack of response. It was this observation which, in many cases, led to the recognition of the syndrome.

Radiographs initially showed patchy areas of consolidation. Thirteen of the 17 cases had serial radiography, and in all of these rapidly developing translucent areas soon were seen. In the majority these were bilateral. Eight of these cases eventually presented radiological evidence of tension pneumothorax with empyema and came to operation.

In four additional cases, all in infants, the presence of abscess, bronchopleural fistula and empyema was not established clinically, but was demonstrated at autopsy.

The development of this complication was rapid but nonetheless insidious and difficult to recognize. The patient was in every case critically ill with respiratory distress and cyanosis; the development of fistula, pneumothorax, and empyema frequently caused little obvious change in the patient's condition.

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## BACTERIOLOGY

From the eight cases which came to operation and four additional post-mortem cases, adequate material was obtained for bacteriological study. Three additional cases with the clinical picture of penicillin-resistant pneumonia and positive x-ray findings had sputum or nasopharyngeal swabs submitted; all showed a heavy growth of *Staphylococcus pyogenes*. *In vitro* sensitivity tests, with one exception, showed resistance to penicillin. In all cases the organism was sensitive to chloramphenicol. Some organisms were sensitive to other broad-spectrum antibiotics.

In one case the patient, who recovered, exhibited clinical evidence of response to chloramphenicol, and the initial *in vitro* sensitivity tests confirmed that we were dealing with an organism sensitive to this drug. During convalescence, cultures taken from the healing empyema sinus showed *Staphylococcus pyogenes* no longer sensitive to this drug. This is significant. Not only does it appear to confirm the micro-evolutionary powers of the organism, but it also suggests most strongly that, wherever possible, the choice of antibiotic should be based upon sensitivity studies.

## MORTALITY

In this series of 17 cases there were five deaths, a mortality rate of 29%. All deaths were in infants from two to 4½ months old. All came to autopsy. The improvement in mortality which follows early diagnosis and adequate treatment will be noted below.

## PATHOLOGY

Space does not permit a complete review of the pathological material. All showed a patchy pneumonic process with multiple abscess formation, bronchopleural fistula and empyema. Four of the five had other serious lesions which had initially led to hospitalization. The histological studies clearly show that the radiolucent areas which characterized the x-ray findings were the result of abscess formation in the pneumonic patches.

## HISTORICAL

Blumenthal and Neuhof[1] in 1946 gave an excellent description of staphylococcal pneumonia and its complications. In all the cases in their series, lung abscess occurred and they reported a high incidence of pyopneumothorax. Late in their

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series penicillin became available and was employed. In those cases in which it was employed the clinical response was strikingly satisfactory. The widespread availability of penicillin at that time resulted in the virtual disappearance of empyema as a complication of pneumonia, and this was accompanied by a logical neglect of bacteriological studies as a feature of the conduct of these cases. Nonetheless the frequent occurrence of "pneumatoceles" during the course of pneumonia in children was reported by Almklov and Hatoff[4] in 1946. Under prolonged therapy with penicillin these lesions gradually disappeared. More recently the emergence of penicillin-resistant organisms has again brought the problem sharply into focus. In particular the staphylococcus has displayed a remarkable power to adapt itself. Thus in 1951 DePape and McEwen[2] drew attention to this problem. Their report included six cases of staphylococcal pneumonia in infants, all with lung abscess. These authors reviewed the literature concerning the emergence of penicillin-resistant strains of staphylococci and commented particularly on the occurrence of these strains in hospital wards and nurseries. McLetchie,[3] Stewart,[5] and Bloomer *et al.*[6] have each reported a series of cases and their findings are all essentially similar to our own. In the series reported by Stewart and in that reported by Bloomer a high incidence of tension pneumothorax and empyema was recorded. In both these series the organism was identified as a penicillin-resistant strain which was, however, sensitive to one or other of the broad-spectrum antibiotics. Both authors stress the necessity for vigilance in the early diagnosis of these cases, for the early employment of a suitable antibiotic and for a constant awareness of the possibility of the development of tension pyopneumothorax which will require immediate adequate closed surgical drainage. Both authors report a high mortality if these principles are not kept in mind and a significant improvement in results following early diagnosis and adequate treatment. Stewart[5] reported a 50% mortality in those cases in which treatment was inadequate.

These reports and our own experience suggest that staphylococcal pneumonia and empyema in infants and children are increasing in frequency and that many cases are not recognized clinically. We have reason to believe that the true incidence may be much greater than is generally recognized.

## TREATMENT

It is evident that the successful treatment of this condition rests primarily upon early diagnosis. The occurrence of one case in a 16-year-old boy would suggest that no age group is exempt, although the disease predominantly has been recognized in infants and children. It is evident, too, that bacteriological studies and sensitivity tests should be done on all cases of pneumonia and that such studies are mandatory in all cases with clinical evidence of penicillin resistance or where x-ray examination reveals the presence of abscess formation as suggested by translucent areas or "pneumatoceles". While chloramphenicol has been the drug of choice in our series, as in other reported series, the proven adaptability of the staphylococcus would suggest that in the future this observation may not be valid.

Once a diagnosis of staphylococcal pneumonia is suspected or made, the case should be followed up by serial radiographs. It has been noted above that abscesses develop rapidly. Even more rapidly do fistula and tension pneumothorax occur. In our cases this complication occurred as early as the third or fourth day. Even daily radiographs need to be supplemented by more frequent careful clinical examination to detect signs of empyema and tension pneumothorax. It is to be emphasized again that one cannot depend on the general condition of the patient to herald its onset. The prompt use of an exploratory needle should establish the diagnosis. Where x-ray or clinical findings suggest a loculated effusion, repeated exploratory thoracentesis at different sites should be employed.

The recognition of pneumothorax or effusion requires the immediate institution of tube drainage with a closed underwater system to which suction may be added. Intercostal drainage or rib resection may be employed. Bloomer[6] suggests the use of two polyethylene tubes. Whatever the method of drainage, it must be adequate. The fluid encountered contains a large amount of thick viscid mucoid material, and small tubes block easily. In two of our cases where intercostal drainage with small tubes gave rise to technical difficulties, rib resection and the insertion of a larger tube were followed by a satisfactory result.

In the treatment of empyema complicating staphylococcal pneumonia there is absolutely no place for the employment of repeated aspiration

as a method of treatment, and no justification for delay in the institution of early surgical drainage. The universal finding of evidence of bronchopleural fistula in the operative and autopsy cases validates this observation.

### RESULTS OF TREATMENT

In 13 of the 17 cases reported here the diagnosis was established clinically and adequate treatment employed. Only one death occurred in this group, a mortality rate of 7.7%. A 4½-month-old-child died despite the employment of properly selected antibiotics and the prompt recognition and drainage of an empyema. Autopsy confirmed the presence of empyema and bronchopleural fistula communicating with a lung abscess. At autopsy seven additional unruptured lung abscesses were identified.

In four cases of staphylococcal pneumonia in this series, multiple abscesses developed which were not complicated by fistula and empyema. These patients recovered, but follow-up radiographs have shown persistent translucent areas. It is our belief that these represent residual abscesses, sterilized by the employment of antibiotics. The experience of Almklov and Hatoff[4] in the era in which penicillin-resistant organisms prevailed would suggest that these lesions may ultimately disappear. These cases are being followed up. In one additional case the abscess appears to have resolved. A long period of observation will be required to determine what sequelæ, if any, will occur.

### CONCLUSIONS

1. Staphylococcal pneumonia is characterized by the rapid development of lung abscess.
2. Bronchopleural fistula with tension pneumothorax and empyema is a frequent complication.
3. Penicillin-resistant strains of staphylococci are frequently the causative organisms; this is particularly the case in hospitalized children.
4. Early diagnosis and adequate treatment by a properly selected antibiotic and the prompt surgical treatment of complicating empyema can bring about a dramatic reduction in mortality.
5. In the series presented, chloramphenicol was the most effective drug; *in vitro* sensitivity tests are essential to determine the drug of choice in the individual case. Rapid changes in drug sensitivity may occur.

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# ANÆSTHETIC AND OPERATIVE PROBLEMS IN THE GERIATRIC PATIENT*

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"ANY ANÆSTHETIC or method, or combination of anæsthetics and methods, that is serviceable and good at all, is serviceable and good for old people. The main difference is that these people are tender, are quieted easily with sedatives, are anæsthetized and relaxed easily and overdosed readily. What they require particularly is conservatism with a little daring mixed in, but with unceasing vigilance and nicety and exactness of administration and control."[1] In these few words Dr. Ralph Knight succinctly portrays the attitude which the anæsthesiologist should adopt toward the care of the aged.

It is the purpose of this paper to discuss the problems encountered in 556 patients 65 years of age and over (Table I) who were subjected to 605 surgical procedures (Table II) at the Duke University Hospital during the 19-month period ending March 1955. Thirty patients had two operations; five had three and three had four interventions. The oldest patient anæsthetized was 100 years.

### PREOPERATIVE ASSESSMENT

Many patients in the older age group present sociological as well as pathological problems. Perhaps our ability to make useful citizens of older people has not kept pace with the in-

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TABLE I.

AGE AND SEX OF PATIENTS

| *Years* | *Number* | *Per cent* | *Sex* | *Number* | *Per cent* |
|---|---|---|---|---|---|
| 65 - 69 | 266 | 47.8 | Female | 233 | 41.9 |
| 70 - 74 | 183 | 32.9 | Male | 323 | 58.1 |
| 75 - 79 | 74 | 13.3 | Total | 556 | 100.0 |
| 80 - 84 | 20 | 3.6 | | | |
| 85+ | 13 | 2.4 | | | |
| Total | 556 | 100.0 | | | |

creased longevity which exists. Many older people who become sick have lost the will to live, and this is reflected in the rather negative attitude which may be adopted towards a surgical procedure. It is of great importance to approach these patients as individuals, not as just a carcinoma of the stomach or a diabetic gangrene. Time must be spent with them to point out their importance to society and the necessity of the forthcoming operation.[2] A patient who wants to get well is more likely to get well.

TABLE II.

TYPE OF OPERATION

| *Type* | *Number* | *Per cent* |
|---|---|---|
| Genito-urinary | 137 | 22.6 |
| Plastic | 79 | 13.0 |
| Intestinal | 50 | 8.2 |
| Gallbladder or common bile duct | 37 | 6.1 |
| Orthopædic | 37 | 6.1 |
| Gynæcological | 35 | 5.9 |
| Amputations | 30 | 4.9 |
| Neurosurgical | 28 | 4.6 |
| Gastric resection | 27 | 4.4 |
| Repair hernia | 26 | 4.3 |
| Thoracic | 24 | 4.0 |
| Radical mastectomy | 17 | 2.9 |
| Eye, E.N.T. | 16 | 2.7 |
| Exploratory laparotomy | 14 | 2.3 |
| Thyroidectomy | 13 | 2.2 |
| Miscellaneous | 35 | 5.8 |
| Total | 605 | 100.0 |

As older age approaches, one of the factors the body becomes deficient in is elasticity.[3] This lack is reflected in the cardiovascular, respiratory and renal systems particularly. The resulting *inherent* hazards to operation are arteriosclerosis, coronary sclerosis, hypertension, emphysema, pulmonary fibrosis and renal insufficiency. They bring in their train the more specific threats of myocardial infarction, cerebrovascular accident and thrombosis or embolism in any part of the body. Every older patient possesses these hazards to a degree, but since age progresses at different rates of speed, some will pose greater problems than others. In the present series (Table III), the resting systolic blood pressure was greater than 160 mm. Hg in 46% of patients. Radiographic enlargement of the heart was seen in 20%, while abnormalities of the electrocardiogram, usually consistent with conduction defects or myocardial disease, were seen in 38%. Problems relating to ventilation were seen in 36% of the patients. When more than one of these evidences of aging was present, the problem became more challenging to the internist, surgeon and anæsthetist.

TABLE III.

PRE-EXISTING DISEASE (INHERENT)

| | *Number* | *Per cent* |
|---|---|---|
| Blood pressure > 160 systolic | 202 | 37.0 |
| Blood pressure > 200 systolic | 54 | 9.7 |
| Pulmonary emphysema or fibrosis | 199 | 36.0 |
| Cardiomegaly | 114 | 20.0 |
| Cardiac arrhythmias | 86 | 15.5 |
| Abnormal electrocardiogram | 212 | 38.1 |
| Previous cerebral accident | 11 | 1.9 |

Certain other complications affect the surgical risk of the older patient. They may be called *acquired* in that they are not necessarily part of the natural process of aging (Table IV). The ravages of carcinoma, apart from the specific lesion for which surgery is being done, are unknown. Whether the presence of this disease is an operative hazard in itself is difficult to say

TABLE IV.

PRE-EXISTING DISEASE (ACQUIRED)

| | *Number* | *Per cent* |
|---|---|---|
| Carcinoma | 200 | 36.0 |
| Malnutrition | 33 | 6.0 |
| Hæmoglobin < 11.0 g.% | 86 | 15.5 |
| Diabetes mellitus | 31 | 5.5 |
| Liver dysfunction | 11 | 1.9 |
| Pernicious anæmia | 6 | 1.0 |

in the light of present knowledge. Malnutrition as an obvious clinical entity was noted in only 6% of patients. It is probable that this deficiency was present in many other patients as well, as may be inferred from the larger number who had a significant anæmia. Cole[4] states that malnutrition is one of the most serious deficiencies to be found in the older patient and greatly increases the hazard of operation. One method of objectively determining such lack of tissue integrity is to measure the blood volume.[5, 6] There is no doubt that correction of blood volume deficits before operation improves the operative and postoperative course of patients.

Much information can be gleaned concerning operative risk from a careful history and physical examination. A review of the day-to-day routine of the patient often will give one an excellent estimate of his cardiac and pulmonary reserve. Discussion of his eating habits and exactly how much he eats each day may give one a lead to his state of nutrition. If his illness is concerned primarily with the alimentary tract, malnutrition is almost certain to exist. When facilities are available, a radiograph of the chest and an electrocardiogram, along with blood chemistry and blood volume studies, are desirable. One should beware the patient who has been confined to bed for more than three or four days. For his proper evaluation all the clinical and laboratory help possible is needed.

Premedication for the geriatric patient must be commensurate with the decrease in his basal metabolic rate. Sedation is important, but should be measured in accordance with his degree of mental and physical prowess. If a patient comes to the operating room "snowed under" with premedication, as reflected by deep sleep, hypotension and slow respiratory rate, one should not hesitate to delay or postpone the operation.

### Operative Management

As noted in the opening paragraph, the anæsthetic management of the older patient differs from that of others not so much in the drugs employed, but in the manner and quantity in which they are administered. The aim is to provide safe anæsthesia and at the same time the best operating conditions for the surgeon, so that the procedure can be completed with dispatch. Safe anæsthesia means light anæsthesia. Safe anæsthesia means adequate pulmonary ventilation so that oxygen will reach the blood stream and carbon dioxide be eliminated properly. Good operating conditions mean adequate relaxation for any surgical intervention.

Probably the greatest error in anæsthesia today is the employment of deep planes of anæsthesia when these are not required. With older patients more susceptible to anæsthetic drugs, it is particularly easy to slip into profound planes of anæsthesia. One can and should provide adequate relaxation with the patient in light, safe planes of anæsthesia. This can be achieved by the judicious use of muscle relaxant drugs.

TABLE V.

ANÆSTHETIC TECHNIQUES EMPLOYED

| | *Number* | *Per cent* |
|---|---|---|
| General anæsthesia | 393 | 64.9 |
| Spinal analgesia | 191 | 31.6 |
| Regional analgesia | 21 | 3.5 |
| Total | 605 | 100.0 |

In Table V it is seen that in this series the greatest number of patients were given general anæsthesia, although spinal and regional analgesia were not neglected. These anæsthetics were given for the most part by residents in training who were under close supervision. Some were given by trained nurse anæsthetists.

TABLE VI.

DRUGS AND TECHNIQUES FOR GENERAL ANÆSTHESIA

| | *Number* | *Per cent* |
|---|---|---|
| Nitrous oxide | 233 | 59.3 |
| Ethyl ether | 212 | 53.9 |
| Pentothal sodium | 175 | 44.5 |
| Ethylene | 111 | 28.2 |
| Meperidine (demerol) | 62 | 15.7 |
| Cyclopropane | 42 | 10.7 |
| Trichlorethylene | 17 | 4.3 |
| Vinyl ether | 14 | 3.5 |
| Anectine | 242 | 61.5 |
| Curare | 15 | 3.8 |
| Flaxedil | 10 | 2.5 |
| Intubation | 268 | 68.4 |
| Assisted respiration | 238 | 60.5 |
| Controlled respiration | 100 | 25.4 |

Table VI indicates that a wide variety of drugs was employed for general anæsthesia. An ultra-short-acting barbiturate, usually thiopentone (Pentothal) sodium, was used to provide a quiet smooth induction in almost every case. In 175 cases it was also used to help maintain anæsthesia. Such drugs are safe for the elderly patient *provided* one realizes that a little bit may

go a long way. Often 75 mg. in a patient 70 years old will produce as much hypnosis and depression as will 500 mg. in a patient 40 years old. Pentothal sodium is a dangerous drug unless the anæsthetist is meticulous in its administration. It can easily produce severe respiratory depression and marked degrees of hypotension.

Induction of anæsthesia should be gradua and take several minutes. Time should be allowed for accommodation of the patient to the first doses of anæsthetic drugs. Blood pressure should be noted carefully. A marked hypotension during a careful induction may well indicate that the blood volume of the patient is low, and that he has been compensating to the best of his ability before anæsthesia began. Serious consideration should be given in these cases to postponing the operation until this condition can be rectified. To proceed is dangerous. After the patient is stabilized, relaxation for intubation may be provided safely with a muscle relaxant, preferably Anectine, 30 to 60 mg. intravenously, if the anæsthetist is prepared and able to augment or control the respiratory exchange of the patient.

Anæsthesia can be maintained with one or several drugs. As noted above, the important factors are to maintain light anæsthesia, good alveolar ventilation and satisfactory operating conditions, i.e., good muscular relaxation when required. Light anæsthesia was assured in most cases by employing a partial rebreathing or non-rebreathing technique. High flow rates of gases, from five to ten litres per minute, always with at least 25% oxygen in the mixture, allowed such a blow-off with each expiration that it was difficult to reach deep planes of anæsthesia, even with potent drugs like ethyl ether. In about half the cases analgesia was reinforced with ethyl ether, and this drug was vapourized to the patient by means of nitrous oxide or ethylene, along with oxygen. It was felt that cyclopropane should not be used when arrhythmias were present or conduction disturbances noted in the electrocardiogram. The use of such a drug, with its propensity to initiate arrhythmias, would tend to confuse the situation.

In about 30% of cases it was desirable to employ the cautery, and in these instances a non-explosive combination of Pentothal and nitrous oxide-oxygen was used. To reinforce the analgesia, meperidine in a continuous drip, utilizing a solution containing 0.5 mg. per c.c.,[7] or trichlorethylene was added frequently.

Adequate alveolar ventilation was assured by watching constantly the movements of the patient's chest with a hand on the reservoir bag of the anæsthetic gas machine. Never was there any hesitation in assisting the respirations of the patient when thought necessary. As seen in Table VI, respiration was assisted or controlled during the greater part of the operation in about 85% of cases. The only contraindication to controlled respirations was felt to be severe shock, when the added positive pressure within the thorax might decrease venous return to a dangerous degree.

Rather than obtain muscular relaxation with deep planes of anæsthesia, muscular relaxant drugs were employed in conjunction with light planes. Anectine (succinylcholine) was used most frequently (61.5%) because it was felt to be controllable easily when used as an intermittent dilute drip of 0.1% solution in 5% dextrose and water. In two patients who received Anectine, respiratory paralysis was prolonged for 55 and 45 minutes beyond the period of operation. In both these patients controlled respiration was maintained during operation. No latent effects were noted from this complication during convalescence. Our experience with succinylcholine leads us to believe that it is a safe drug to employ when the anæsthetist is prepared and able to assist or control respirations in a proper manner.

Spinal analgesia was found useful for lower trunk and lower extremity procedures (Table V.) With few exceptions Pontocaine was the drug employed (Table VII). In the majority of cases a hyperbaric solution weighted with dextrose was used, following the Sise technique. The hypobaric solution consisted of 20 mg. of Pontocaine dissolved in 20 c.c. of distilled water (0.1% solution). In about half the cases, epinephrine 0.25 to 0.5 mg. was added to the spinal anæsthetic solution, and this served to prolong analgesia significantly.

TABLE VII.

SPINAL ANALGESIA

| | *Number* | *Per cent* |
|---|---|---|
| Pontocaine | | |
| Hyperbaric | 161 | 84.3 |
| Hypobaric | 21 | 11.0 |
| Isobaric | 9 | 4.7 |
| | 191 | 100.0 |
| Vasopressor in spinal solution | 99 | 51.8 |

In all patients, regardless of the previous blood pressure, 25 to 50 mg. of ephedrine sulphate was injected subcutaneously with the local procaine wheal before subarachnoid injection. No abnormal hypertensive phenomena were seen. It was felt more desirable to have a small rise in blood pressure than a pronounced fall after induction of the analgesia.

Regional analgesia was chosen for only 21 patients, but a variety of block procedures were performed (Table VIII). Block of the ilio-

TABLE VIII.

REGIONAL ANALGESIA

| | |
|---|---|
| Herniorrhaphy block | 6 |
| Intercostal block | 6 |
| Epidural block | 4 |
| Caudal block | 3 |
| Brachial block | 1 |
| Abdominal field block | 1 |
| Total | 21 |

inguinal and iliohypogastric nerves was found useful for herniorrhaphy in the aged. Bilateral intercostal block was a method of choice for exploratory laparotomy in the extremely poor-risk patient. Xylocaine and cyclaine were the two local anæsthetic drugs employed for these procedures. No toxic reactions were seen in this group of patients.

Complications and therapy applied during operation are noted in Table IX. Almost 50%

TABLE IX.

COMPLICATIONS AND THERAPY DURING OPERATION

| *General anæsthesia* | *Number* | *Per cent* |
|---|---|---|
| Hypotension requiring therapy | 56 | 14.3 |
| Arrhythmias | 5 | 1.3 |
| Prolonged apnœa | 2 | 0.5 |
| *Spinal analgesia* | | |
| Hypotension requiring therapy | 34 | 17.8 |
| Supplemental sedation | 59 | 30.9 |
| *Regional analgesia* | | |
| Hypotension requiring therapy | 3 | 14.3 |
| Supplemental sedation | 11 | 52.4 |
| Transfusions | 260 | 46.7 |

of patients received one or more bottles of blood during operation. It was felt that the best way of avoiding shock was to anticipate it and replace blood as it was being lost on the table. We did not wait for changes in pulse rate or blood pressure before beginning a transfusion. Blood was pumped in by syringe when it was felt necessary. A total of 93 patients (16.7%) suffered a degree of hypotension during operation which required therapy. In some patients the fall in pressure was due to blood loss, in some to abnormal reflex activity, in others to deep anæsthesia or inadequate ventilation. In most of the cases under spinal analgesia the hypotension was due to paralysis of the sympathetic nervous system induced by the subarachnoid injection. In all patients an intravenous drip of 5% dextrose in water was begun before inducing anæsthesia, so that a ready avenue for injection of drugs was available constantly.

Supplementary sedation was provided in 70 cases of spinal and regional analgesia. The intravenous administration of secobarbital, 50 mg., pentobarbital, 50 mg., or meperidine as a continuous drip infusion (0.5 mg. per c.c.), was tolerated well by patients. In a few instances general anæsthesia was necessary.

The length of operation is of importance in the older age group. If anæsthesia lasts longer than two hours, the risk to the patient increases and the task of the anæsthetist becomes more exacting. The duration of anæsthesia in the present series is found in Table X. In many lengthy pro-

TABLE X.

LENGTH OF ANÆSTHESIA

| | *Number* | *Per cent* |
|---|---|---|
| Less than 2 hours | 316 | 52.2 |
| Less than 3 hours | 150 | 24.8 |
| Less than 4 hours | 84 | 13.9 |
| More than 4 hours | 55 | 9.1 |
| Total | 605 | 100.0 |

cedures an endotracheal tube is inserted to be certain that an unobstructed airway persists for the entire procedure.

### POSTOPERATIVE ASSESSMENT

Careful transfer from the operating table to bed and to the recovery room, expert nursing care in the recovery room, early awakening and early ambulation are important in any patient, but particularly in the elderly. Towards the end of a long operation it is of some value to inject intramuscularly a vasopressor (desoxyephedrine, 10 mg.) to counteract the probable fall in blood pressure which may occur with movement. It is important to verge on cruelty in the postoperative care of the elderly patient. Narcotics and sedatives should be reduced to a minimum. The stir-up regimen should be in full force. Thrombo-

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TABLE XI.

| POSTOPERATIVE MORBIDITY | | |
|---|---|---|
| *Respiratory* | | |
| Pneumonia | 5 | |
| Atelectasis | 4 | |
| Pneumothorax | 1 | |
| Total | — | 10 |
| *Electrolyte imbalance* | 8 | |
| Total | — | 8 |
| *Thrombo-embolism* | | |
| Leg | 2 | |
| Pulmonary | 2 | |
| Cerebral | 3 | |
| Coronary | 1 | |
| Total | — | 8 |
| Cardiac arrhythmias | 4 | |
| Psychosis | 3 | |
| Wound infection | 2 | |
| Shock | 2 | |
| Convulsions | 1 | |
| Renal infection | 1 | |
| Nerve palsy | 1 | |
| Patient's disease | 1 | |

embolism and atelectasis with pneumonia are fostered by the over-solicitous nurse or relative.

In the present series significant postoperative morbidity occurred in 36 cases (6.5%) (Table XI). Electrolyte imbalance was combined with respiratory complications in several patients. The largest number of complications were respiratory, and it is believed that more vigorous therapy in the postoperative period might have prevented their development. Seven of the eight patients who developed electrolyte imbalance postoperatively had had intra-abdominal procedures. Four of these patients suffered a wound dehiscence eight to 10 days after operation.

TABLE XII.

| POSTOPERATIVE MORTALITY | | |
|---|---|---|
| *Thrombo-embolism* | | |
| Coronary | 3 | |
| Cerebral | 3 | |
| Pulmonary | 1 | |
| Aorta | 1* | |
| Total | — | 8 |
| *Infection* | | |
| Electrolyte imbalance | 6 | |
| Total | — | 6 |
| *Respiratory* | | |
| Obstruction | 1* | |
| Failure | 1* | |
| Atelectasis | 1 | |
| Pneumonia | 1 | |
| Total | — | 4 |
| Renal failure | 1* | |
| Myocardial failure | 1* | |
| Patient's disease | 1 | |

*Could be classified under patient's disease.

One patient developed hæmorrhagic shock 12 hours after operation, and another developed sudden, unexplained shock five days after operation. Both required vigorous therapy, the first with blood and the second with blood and vasopressors.

In this series nobody died in the operating room. Twenty-one patients (3.7%) died in the postoperative period while in hospital. Table XII summarizes the causes of death which occurred between 16 hours and 44 days after operation. The causes with an asterisk beside them could be grouped under "patient's disease", because in each instance the reason for death was preexistent to a major degree in the patient before operation.

In this series thrombo-embolic phenomena were the commonest cause of death. It appears important to maintain circulation in a rigorous manner postoperatively and to make the patient move about as much as possible. Infection and its associated electrolyte imbalance accounted for six deaths. The elderly patient has little reserve to fight infection after a major operation.[8] Moreover, the antibiotic spectrum is not yet complete for intestinal flora. Respiratory deaths are becoming less common, and this may be due in part to the bolder approach to potential respiratory infection in the postoperative period. When secretions are abundant and the patient is having difficulty in clearing his lungs, serious consideration should be given to performing a tracheotomy. This is particularly useful after thoracic operations.

A résumé of the deaths following operation is appended. In none was it felt that anæsthesia was a major contributing factor. In spite of the numerous preoperative complications present in this series of patients, it is of interest that "cardiac arrest" was not an initiating element in any death.

1. M., 68 years. Death 16 hours. Traumatic fracture dislocation C5-C6. B.P. 130/70. Hb. 14.5 g. Heart normal. Spinal fusion C2 to C7. Transtracheal, nasotracheal awake, pentothal 325 mg., nitrous oxide, oxygen, trichlorethylene, 1,500 c.c. blood. Anæsthesia uncomplicated, 3½ hours. Patient did well for 12 hours, then developed respiratory obstruction. Tracheotomy of some help, but course downhill, and patient died of respiratory failure. Death believed due to patient's disease.

2. F., 70 years. Death 16 hours. Chronic tuberculous lung abscess. B.P. 120/76. Hb. 11.0 g. Heart normal. Right upper lobectomy. Ethylene-oxygen 4:1.5, ethyl ether, Anectine, 450 mg., orotracheal, controlled respirations. 2,000 c.c. blood. Hypotension on one occasion during 3½-hour operation. Had severe hypotension six

hours postoperatively, which responded to blood; 16 hours after operation suddenly went into profound shock and died. Death believed due to pulmonary embolism.

3. M., 86 years. Death 24 hours. Benign prostatic hypertrophy. B.P. 200/110. Hb. 12.4 g. Cardiomegaly. Electrocardiogram normal. Emphysema. Perineal prostatectomy. Continuous spinal Pontocaine 13 mg. with dextrose. Demerol, 100 mg., Seconal 150 mg. 1,000 c.c. blood. Anæsthetic course normal, 2¾ hours. Did well for 24 hours, then sudden profound hypotension, pulmonary œdema and death occurred. Death believed due to coronary thrombosis.

4. M., 73 years. Death 48 hours. Thrombosis popliteal artery. B.P. 180/80. Hb. 12.8 g. Diabetes. Emphysema. Old supracondylar amputation. Supracondylar amputation remaining leg. Spinal Pontocaine 10 mg. with dextrose, supplemented with Pentothal, 125 mg., nitrous oxide, oxygen, demerol, 50 mg. Anæsthetic course normal, 2¼ hours. Postoperatively satisfactory for 24 hours, then went into profound shock. Electrocardiogram showed recent coronary thrombosis. Autopsy showed almost completely occluded coronary vessels.

5. M., 72 years. Death 48 hours. Tuberculous pericarditis. Malnutrition. Increased venous pressure. Electrocardiogram: auricular and ventricular premature beats, abnormal T-wave changes. Cardiac decompensation. B.P. 88/70. Hb. 13.2 g. Thoracotomy, pericardiectomy. Ethylene-oxygen 4:1.5, cyclopropane (trace), ethyl ether (trace), Anectine 40 mg., orotracheal, controlled respirations. Stormy operative course with arrhythmias, Neosynephrin drip, hypotension to 50/40/mm. Hg. on several occasions. 1,000 c.c. blood. Anæsthesia three hours. Satisfactory postoperative course for 36 hours, then rapidly progressing cardiac failure and death. Death believed due to patient's disease.

6. M., 72 years. Death 72 hours. Saddle embolus for 30 hours. B.P. 170/100. Hb. 14 g. Coronary thrombosis 10 days previous. Electrocardiogram: auricular fibrillation, evidence of recent anterior infarction. Embolectomy. Continuous spinal Pontocaine 8 mg. with dextrose. 500 c.c. blood. Anæsthetic course normal, 1½ hours. Postoperatively embolism or thrombosis recurred, with death in 72 hours. Death due to patient's disease.

7. M., 76 years. Death 96 hours. Bilateral gangrene legs. B.P. 160/80. Hb. 12.9 g. Emphysema. Cardiomegaly. Electrocardiogram: auricular fibrillation. Bilateral supracondylar amputations. Spinal Pontocaine, 11 mg. with dextrose. 500 c.c. blood. Severe hypotension on one occasion. Anæsthesia 1½ hours. Postoperative course satisfactory for four days, then cerebrovascular accident developed and rapid demise ensued.

8. M., 69 years. Death 96 hours. Carcinoma pancreas with jaundice. B.P. 130/80. Hb. 13.2 g. Liver enlarged. Exploratory laparotomy, cholecyst jejunostomy. Ethylene-oxygen 4:1.5, ethyl ether, Anectine 160 mg., orotracheal, assisted respirations. Anæsthesia 2½ hours. Postoperatively did well for three days, then developed fever to 40° C. and died in 24 hours. Death believed due to peritonitis.

9. M., 69 years. Death five days. Carcinoma lung. B.P. 190/90. Hb. 12 g. Emphysema. Pulmonary function 62% of normal. Electrocardiogram: left axis deviation, wide Q R S - T angle, evidence of old myocardial infarction. Thoracotomy, left upper lobectomy. Pentothal, 200 mg., cyclopropane, ether (trace), Anectine, 200 mg., orotracheal controlled respirations. 1,000 c.c. blood. During anæsthesia labile blood pressure possibly due to low blood volume. Anæsthesia, 2½ hours. Postoperatively patient showed atelectasis right upper lobe. Lethargy developed with no will to live or help himself. Terminal aspiration and atelectasis.

10. F., 67 years. Death six days. Ten days previously had resection of ileum and ileocecostomy for mesenteric thrombosis. At time of operation, had wound dehiscence and infarction ascending colon. B.P. 180/80. Hb. 10.1 g. Severe electrolyte imbalance. Emphysema. Cardiomegaly. Electrocardiogram: left bundle branch block, premature ventricular beats. Right colectomy, ileostomy, colostomy, closure of wound dehiscence. Pentothal, 75 mg., ethylene-oxygen 4:1.5, ether (trace), Anectine, 10 mg., demerol, 75 mg., orotracheal, assisted respirations. 1,000 c.c. blood. Hypotension on three occasions during operation. Anæsthesia, two hours. Postoperatively did poorly. Electrolyte imbalance continued, terminal hypostatic pneumonia. Death due to patient's disease.

11. F., 65 years. Death eight days. Carcinoma thyroid. B.P. 152/90. Hb. 10.3 g. Dyspnœa, respiratory obstruction. Heart normal. Partial excision thyroid, tracheotomy. Pentothal, 1,100 mg., ethylene-oxygen 4:1.5, Anectine, 300 mg., orotracheal, controlled respirations. 500 c.c. blood. Anæsthetic course uneventful, 1¾ hours. Recovered fully from operation. Developed increasing respiratory obstruction in seven days and died 24 hours later. Death due to patient's disease.

12. M., 66 years. Death nine days. Aneurysm left iliac artery. Obstruction of colon. Right upper lung infiltration. B.P. 140/100. Hb. 12.5 g. Electrocardiogram: myocardial ischæmia. Excision aneurysm, left iliac artery. Pentothal, ethylene-oxygen 4:1.5, ether, orotracheal, controlled respirations. Massive hæmorrhage during operation with hypotension five times. 4,000 c.c. blood. Postoperatively developed gangrene left leg. Died nine days from "toxic" absorption.

13. M., 84 years. Death nine days. Carcinoma stomach with obstruction. B.P. 180/90. Hb. 4.5 to 12.0 g. at operation. Cardiomegaly. Electrocardiogram: first degree heart block, premature ventricular beats, S T depression. Gastric resection. Intercostal nerve block, bilateral, splanchnic block. Xylocaine, 500 mg. Hypotension on one occasion. Anæsthesia, 2¼ hours. Did well for several days. Cerebrovascular accident developed nine days after operation, with rapid death.

14. M., 71 years. Death nine days. Resection carcinoma sigmoid nine days previously. At operation, had abscess presacral area. B.P. 205/110. Hb. 12.0 g. Comatose, uræmia, electrolyte imbalance. Condition critical. Abdominal drainage of abscess. Ethylene-oxygen 4:1.5, ether (trace), cyclopropane. Anæsthesia, 30 min. Condition remained critical and patient died nine days after this operation. Death due to infection.

15. F., 65 years. Death 11 days. Bilateral renal calculi. Pyelonephritis. B.P. 136/60. Hb. 6.8 to 12.5 g. at operation. N.P.N. 120. Cardiomegaly. Electrocardiogram: normal. Excision fissure-in-ano. Caudal block with cyclaine, 440 mg. Seconal, 50 mg. i.v. Anæsthesia uncomplicated, one hour. Died 11 days postoperatively in uræmia. Death due to patient's disease.

16. M., 91 years. Death 14 days. Intestinal obstruction, seven days. B.P. 190/110. Emphysema. Premature ventricular beats. Exploratory laparotomy (no obstruction found). Pentothal, 75 mg., ethylene-oxygen 4:1.5, ether. Anæsthesia satisfactory, 1¼ hours. Did well for several days, then developed lobar pneumonia, auricular fibrillation and recurring abdominal distension. Death due to patient's disease.

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17. Death 17 days. Carcinoma lung. B.P. 135/75. Hb. 12.5 g. Electrocardiogram: normal. Right pneumonectomy. Pentothal, 300 mg., ethylene-oxygen 4:1.5, ether, Anectine, 400 mg., orotracheal, controlled respirations. 1,700 c.c. blood. Anæsthesia course satisfactory, six hours. Developed cerebrovascular accident 12 hours postoperatively and bronchopneumonia later.

18. F., 66 years. Death 24 days. Fibrosis sphincter Oddi. B.P. 140/80. Hb. 12.5 g. Emphysema. Electrocardiogram: normal. Re-exploration of common bile duct; duodenotomy. Pentothal, 800 mg., nitrous oxide, oxygen 5:2, demerol, 125 mg., curare, 21 mg., orotracheal, assisted respirations. 500 c.c. blood. Anæsthetic course uneventful, 3½ hours. Postoperatively developed electrolyte imbalance and myocardial infarction on fifth day.

19. M., 72 years. Death 24 days. Obstructive duodenal ulcer and hæmorrhage. B.P. 120/80. Hb. 15.0 g. Dehydrated, malnutrition. Asthma and emphysema. Electrocardiogram: left axis deviation. Subtotal gastric resection. Ethylene-oxygen 4:1.5, ether, Anectine, 250 mg., orotracheal, spontaneous respiration. Hypotension on three occasions during operation, believed due to low blood volume. 1,500 c.c. blood given. Anæsthesia time, 5½ hours. Postoperatively did poorly and gradually went downhill. Autopsy showed generalized peritonitis and multiple pulmonary abscesses. Death due to infection.

20. M., 77 years. Death 25 days. Carcinoma stomach. B.P. 120/70. Hb. 10.5 g. Malnutrition. Emphysema. Heart normal. Subtotal gastric resection and drainage large subhepatic abscess. Pentothal, 250 mg., cyclopropane, Anectine, 400 mg., orotracheal, controlled respirations. 500 c.c. blood. Anæsthetic course smooth, three hours. Developed large draining sinus and associated electrolyte imbalance. Death due to infection.

21. M., 69 years. Death 44 days. Carcinoma pancreas with jaundice. B.P. 140/80. Hb. 14.5 g. Electrocardiogram: old posterior infarct. Exploratory laparotomy and exploration common bile duct. Ethylene-oxygen 4:1.5, ether, Flaxedil, 210 mg., orotracheal, assisted respirations. 500 c.c. blood. Anæsthetic course satisfactory, 5¾ hours. Postoperatively ran gradual downhill course with terminal bronchopneumonia. Death due to patient's disease.

SUMMARY

1. An analysis is presented of 556 patients over 64 years of age who were subjected to 605 operations during the 19-month period ending March 1955.

2. Anæsthetic and operative management is discussed.

3. Significant postoperative morbidity occurred in 36 patients (6.47%).

4. Twenty-one patients (3.7%) died after operation while in hospital. A brief summary of these cases is presented and the causes of death are enumerated.

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# IRRADIATION OF BLADDER CARCINOMA BY THE FRIEDMAN-LEWIS TECHNIQUE*

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AFTER REVIEWING the results of treatment of carcinoma of the bladder by irradiation, one can justifiably be rather pessimistic about the benefits achieved to the present time. It is not felt necessary to review again these unsatisfactory results, since the subject was well covered by Duff and Hyman[1] in 1951, when they reported their results with the use of the "intravesical radium bomb".

The study which forms the basis of this paper was undertaken following publication in 1949 of a rather optimistic report by Friedman and Lewis,[2] in which they described the technique and results of a method of radium treatment of bladder tumours which they had evolved. This method provided for irradiation of the bladder by means of a 25 mg. radium tube suspended in the lumen of a 30 c.c. Foley catheter, the urine being drained from the bladder by means of a suprapubic tube. The bag was sufficiently distended to hold the bladder wall at least 2.0 cm. from the radium tube. The method used by us was the same as that recommended by Friedman and Lewis, with certain modifications, especially as regards the suprapubic drainage of the bladder.

Suprapubic cystotomy was not performed as a routine for drainage of the bladder, unless it was

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found impossible to resect the tumour to the level of the mucosa transurethrally. The bladder was drained through the lumen of the Foley catheter, the urine passing around the radium tube. The most satisfactory catheter for this purpose was found to be the No. 24 F. 30 c.c. Foley "radium" catheter, manufactured by Bard. This catheter has a relatively large lumen and the majority of the bags will distend evenly, allowing for more even distribution of the irradiation. Two 25.0 mg. radium tubes of standard size were changed, the active element being lengthened and the walls being diminished in thickness. After the change these two tubes had the following dimensions and radium content. Each tube was 15.0 mm. in length with an active length of 10.0 mm. The tube wall was of platinum 0.5 mm. in thickness and the outside diameter was 2.5 mm., which allowed for free drainage around the tube. One tube contained 24.65 mg. of radium and the other 24.77 mg., the allowable variation in each being 0.25 mg. Both tubes were calibrated, and at intervals checked by the National Research Laboratories of Canada. It is, of course, well recognized that with such thin screening great care must be exercised to detect any defect in the tube, the presence of which would have disastrous results. These tubes were suspended in the lumen of the catheter by a silk suture in such a way that there was no possibility of movement. The 30-c.c. bags were distended with 42.0 to 44.0 c.c. of 4% NaI, giving an outside diameter of 4.1 to 4.3 cm. The position of the radium in the bag, and the container in the bladder, was checked by anteroposterior and lateral radiographs after insertion. It is appreciated that, because of the slight variation in diameter of the distended bags, there was a slight variation in the dosage of gamma roentgens delivered to comparable areas of the bladder mucosa in different cases. The exposure, except in one case, approximated 4,800 mg. hours, or approximately 8,000 gamma r. In one case only 7,000 gamma r was received, as in several more recent cases not reported in this article. It was also appreciated that any interference with drainage of the urine would lessen the therapeutic effect of the radium, and no case received this therapy when either bloodclot or slough might have caused blockage of the catheter. The routine was an exposure of 4,000 r, a rest of four or five days, and then a further exposure of 4,000 r. The distending medium in the bag was coloured with methylene blue, in order that any rupture of the bag would be immediately recognized by staining of the urinary drainage.

External irradiation was used in only two cases. One of these patients had an extensive adenocarcinoma involving the whole anterior wall of the bladder, and the second had a very extensive involvement with epidermoid carcinoma of the bladder floor and vaginal vault. The latter patient received in addition 2,400 mg. hours of radium therapy *per vaginam*, all irradiation therapy being carried out after ureterointestinal anastomosis. Although there was a marked temporary regression in the tumour, the patient died after an interval of 22 months.

The results of treatment in this series of cases are tabulated in Tables I-IV. It will be appreciated that the classification of bladder tumours is very difficult. As is well known, the depth of penetration into the bladder wall is much more important than the grading of the tumour. In the following cases the extent of the spread was taken into account, so that while they are put into grades, it might be better to regard the latter as various stages. No case has been included in this series which did not have a definite pathological diagnosis of malignancy, and five of these cases were treated in an attempt at palliation only, no hope of cure being entertained.

TABLE I.

GRADE ONE TUMOURS.
(TWO SURVIVING WITHOUT RECURRENCE. AVERAGE SURVIVAL FOR WHOLE GROUP 34.8 MONTHS.)

| *Survival (months)* | *Recurrences* | *Death* |
|---|---|---|
| 1. 23 mos. | +Ureteral | Coronary disease |
| 2. 58 mos. | 0 | |
| 3. 37 mos. | Metastases. No local recurrence. | Carcinoma |
| 4. 9 mos. | Never cleared | Postoperative death |
| 5. 54 mos. | 0 | |
| 6. 28 mos. | 0 | Cardiac disease |

The first patient in the first group (Table I) had an interesting history. In 1943, at 34 years of age, he was operated upon suprapubically and a papilloma of the bladder was resected and fulgurated. In 1947 the left kidney and part of the left ureter were removed for papillary carcinoma. Between 1948 and 1950 he was operated upon 12 times for massive papillary

tumours of the bladder, three times suprapubically and nine times transurethrally. He persistently refused cystectomy. It is estimated that over 350 g. of tissue were removed during the latter period. In April 1950 he received radium therapy. There were only two small recurrences in the next 17 months, one in the dome of the bladder and one at the left ureteral orifice, evidently originating in the stump of the left ureter, as the bladder was found to be fixed in this area on bimanual examination.

TABLE II.

GRADE TWO TUMOURS.
(AVERAGE SURVIVAL FOR GROUP 57 MONTHS.)

| *Survival (months)* | *Recurrences* | *Death* |
|---|---|---|
| 7. 52 mos. | 0 | 0 |
| 8. 60 mos. | 0 | 0 |
| 9. 60 mos. | 0 | 0 |
| 10. 52 mos. | 0 | 0 |
| 11. 48 mos. | ? | 0 |
| 12. 50 mos. | 0 | 0 |

In Case 11 (Table II) the patient had his last check-up at 34 months and is still alive at 48 months, although we do not know whether or not there has been a recurrence.

TABLE III.

GRADE THREE TUMOURS.
(AVERAGE SURVIVAL FOR GROUP 30.8 MONTHS.)

| *Survival (months)* | *Recurrences* | *Death* |
|---|---|---|
| 13. 20 mos. | + | Coronary disease |
| 14. 44 mos. | ++ | Carcinoma |
| 15. 48 mos. | ? | 0 |
| 16. 19 mos. | Never cleared | Carcinoma |
| 17. 23 mos. | Never cleared | Coronary disease |

The patient in Case 15 (Table III) was 81 years of age. He gave a history of intermittent gross hæmaturia for the previous seven years, with great loss of weight and strength. On examination there was a large papillary tumour with areas of ulceration covering the floor of the bladder and the left lateral wall. This was readily palpable on bimanual examination. Intravenous pyelography showed that the left kidney was not functioning. After transurethral resection of the tumour and radium treatment, the patient's condition improved, and 28 months later the patient had complete urinary comfort and no evidence of tumour on cystoscopic examination. At 48 months he reports himself as well, but refuses cystoscopic examination for economic reasons. This patient was considered incurable and was treated in an attempt at palliation only. This latter, at least, seems to have been achieved up to the present time. Case 16 was also very extensive and the period of survival was short.

It is quite well recognized that, in this method of irradiation of bladder tumours, the healthy portion of the bladder wall is subjected to as intense irradiation as is the tumour area. Fortunately, the mature mucosa and underlying structures are more resistant to this effect than is the immature tumour cell. As the maximum irradiation is delivered at right angles to the active element, the floor of the bladder, the main tumour-bearing area, receives the maximum irradiation, but all areas are irradiated to a greater or less extent. Because of this generalized diffusion of irradiation there is danger of

TABLE IV.

GRADE FOUR TUMOURS.

| *Survival (months)* | *Recurrences* | *Death* |
|---|---|---|
| 18. 9 mos. | Never cleared | Carcinoma |
| 19. 22 mos. (Epidermoid carcinoma) | Never cleared | Carcinoma |
| 20. 19 mos. (Adenocarcinoma) | Never cleared | Carcinoma |

damage to the bladder wall, which may be irreparable and lead to a marked bladder contracture. Friedman and Lewis recognized this possibility early in their investigation and reduced the dosage in an attempt to reduce the damage to the normal bladder wall and still deliver a cancerocidal dose to the tumour area. In the course of our investigation we have not been as unfortunate in regard to the development of irradiation cystitis and bladder contracture as have some others.

In view of the adverse reports concerning this most distressing complication of treatment, all patients were checked at periodic intervals with regard to the incidence of cystitis and also as to the bladder capacity. It is difficult to evaluate in any graphical way the severity of the complaints, as they varied greatly from month to month. In some cases there appears to be a periodicity to the symptoms; the patient will be completely free of any complaints for weeks, have a return of urinary frequency and dysuria for a time, and then become asymptomatic again. It does appear that the incidence and the severity of

cystitis have been very much greater in those patients with far advanced carcinoma in which the tumour never appeared to be completely cleared. How much of the cystitis was due to the sloughing tumour and how much was due to the irradiation is difficult to say. Five patients had very slight frequency. Seven had moderate frequency with some suprapubic discomfort and moderate dysuria for periods of several months, gradually decreasing as the tumour area healed. Eight patients had quite marked reactions, with frequency, marked dysuria and hæmaturia. However, as stated before, nearly all of these patients had advanced carcinoma, and it is felt that the sloughing tumour had as much to do with the symptoms as the irradiation. In two cases, however, one with a grade 1 and one with a grade 2 lesion, there were very severe reactions and contractions of the bladder.

The first patient, a male of 58, presented himself in October 1950 with two large papillary tumours of the bladder, grade 1, which were resected transurethrally. He was readmitted to hospital in March 1951, complaining of pain on voiding and frequency of q.1.h. both day and night. In April the bladder was irradiated and his urinary complaints became much more marked. Repeated cystoscopies showed marked inflammation and contraction of the bladder. Uretero-intestinal anastomosis was refused. In January 1952 a uretero-cutaneous anastomosis was carried out at another hospital. The patient died of shock six days after operation.

On reviewing this case it is evident that radium therapy should never have been carried out, because it only seemed to aggravate complaints present to a less degree before treatment.

The second patient, a woman of 58 years, had radium treatment for carcinoma of the cervix 15 years previously. There was no evidence of recurrence of the carcinoma of the cervix. The bladder tumour was a flat infiltrating and ulcerating tumour involving three-quarters of the trigone and classified as grades 2 and 3. It was irradiated in October 1950, and immediately afterwards the patient developed a moderate cystitis which gradually increased in severity. In January 1952, cystoscopy showed a marked cystitis with ulceration on the trigone. Biopsies from this area were negative for tumour, but showed the changes noted in ulceration due to irradiation. Pyelograms showed marked bilateral hydro-ureter and hydronephrosis, and the bladder capacity was only 75 c.c. On standing or walking this patient is partially incontinent, but the dysuria is controlled almost completely by antispasmodics. At the time of writing the patient is still alive with the same clinical picture as above, and with no evidence of tumour recurrence.

The above patient is one of the nine survivors; the remaining eight have little or no bladder discomfort, and very little increase in urinary frequency.

It would seem that the incidence of severe irradiation cystitis has been somewhat less frequent in this small series than has been reported by others. When this complication does occur, however, it is excruciatingly painful and requires diversion of the urine from the bladder, but only after the surgeon is satisfied that it will not clear spontaneously. The woman above claims that she gets complete relief from pain with Donnatol, though of course she still has frequency and partial incontinence. In several of the other cases antispasmodics were of little or no value.

## SUMMARY

Of the 20 patients treated, eight have survived without recurrence for an average of 54.2 months, one has survived for 48 months, and 11 are dead after an average of 23 months.

Of the latter, six died from carcinoma, four from coronary disease, and one postoperatively, although he had a residual tumour. In three of the cardiac deaths, either the patient had a recurrence or the bladder never appeared free of tumour.

## CONCLUSION

It is realized that this series of cases is rather small and that the length of time has not been great. However, the present survival rate compares favourably with that in other published series. It seemed to us that if by this method, plus resection, a cancerocidal dose of radiation could be carried to a depth of approximately 1.0 cm. below the level of the bladder mucosa, with a much wider area of bladder wall covered than by other methods, other than external irradiation, the method was worthy of further trial. Accordingly, a further series of cases has been treated, but the periods of survival are too short for inclusion here.

In this further series the amount of irradiation has been reduced to 6,000-7,000 gamma r, and in advanced cases uretero-intestinal anastomosis has been done, followed by both external and intravesical irradiation. In the latter method, one need not be concerned with the possibility of excess intravesical irradiation, or carry the dosage of external irradiation to the extent where it may lead to bowel complications. Also, following uretero-intestinal anastomosis, extensive carcinoma of the base of the female

bladder may be benefited by added irradiation *per vaginam*.

It might be suggested that resection be carried deeply and widely into the bladder wall and that, in addition, the above method of irradiation be carried out in four to six weeks, or when the slough has separated. It is felt that the incidence of radiation ulceration and cystitis is greater when treatment is carried out immediately after resection. Irradiation is suggested because it is impossible to judge the extent of the tumour during resection, other than in the area where the bladder wall is grossly involved.

We wish to express our appreciation to Dr. J. W. McKay, Director of the Department of Radiology at the Montreal General Hospital, for his helpful co-operation and advice in the treatment of these cases. Further, we wish to thank the Quebec Government, which has made possible the Tumour Registry, without whose help it would have been almost impossible to follow up these patients.

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# HYPERTENSION AND UNILATERAL KIDNEY DISEASE. LATE RESULTS OF NEPHRECTOMY IN SEVEN PATIENTS*

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EVER SINCE Goldblatt's original report[1] and the more recent experiments,[2] great interest has been stimulated in the role of the kidney in human hypertension.

My interest in this condition goes back several years, when the term "malignant hypertension" burst into the medical literature. I recall that at first our diagnoses were made in retrospect at the post-mortem table. Then, two patients died of what turned out to be unilateral kidney disease. One was a 46-year-old man with thrombosis of the renal artery: the other was a male of 27 years of age who had one kidney totally destroyed by tuberculosis, a diagnosis which was a complete surprise. Thus, doubly and amply warned, we were on the lookout to detect cases earlier. At the Montreal General Hospital, we were all stimulated by Dr. Patch's dramatic case in 1939 (Case 1, below). Since that time we have had the opportunity of observing six more patients with long-term follow-up studies.

It is the purpose of this report to review these seven cases of hypertension, associated with unilateral kidney disease, treated by nephrectomy. Especially do I wish to emphasize that there is often a characteristic clinical picture, which if recognized and treated promptly may result in complete cure. The outstanding features of this picture are:

1. A short history of hypertension—often coming as a surprise finding in young people.
2. A rapidly progressive downhill course.
3. Severe headaches and retinopathy.
4. Diastolic pressures of 120 mm. Hg or more.
5. A dramatic result obtained by unilateral nephrectomy if carried out early while the function of the opposite kidney is still normal or nearly so.

The seven cases reported bring out these features in a striking manner.

## CASE REPORTS

1. Mrs. B., age 25.—Mrs. B.'s is the famous case quoted extensively in the literature, and reported by the late Drs. F. S. Patch and L. J. Rhea in 1939.[3]

When she was 12 years old, she was seized with several short convulsions 24 hours after complaining of sudden severe headache. She became unconscious and was admitted to hospital. Hypertension (170/120 mm. Hg) was noted, and diminished function on the right side. A right nephrectomy was performed by Dr. Patch on December 27, 1939. Within one week, the blood pressure fell to 110/70 mm. Hg, where it has remained since. Her health is excellent in every way, and she was married in 1950. The pathological diagnosis was atrophic pyelonephritis.

2. D.J., age 18.—D.J. was admitted in June 1940 for investigation of periodic headaches, hypertension and pyuria. While he was under investigation for a strabismus which developed after a head injury the blood pressure was noted to be 150/90 mm. Hg.

He was well developed and well nourished for his age. In hospital, the blood pressure varied from 166 to 180 systolic and 108 to 110 diastolic. The general physical examination was otherwise negative. The genitourinary investigation revealed radiologically abnormal

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right kidney, and impaired function on that side. The right phenolsulphonphthalein appearance time was delayed and the total excretion of dye in seven minutes was 0.96% compared to 2.3% on the left side.

A right nephrectomy was performed by Dr. Patch on July 15, 1940. Within five days the blood pressure fell to 130/90 mm. Hg. Two months later the blood pressure was normal, 122/80 mm. Hg, where it remained. The pathological diagnosis was chronic atrophic pyelonephritis with an accompanying severe papillitis.

He went to England to live. His mother reports that he was working and in good health, leading an active life until September 1954 when he developed signs of failure of the remaining kidney, and a return of severe hypertension. He died in January 1955, 14½ years after the operation. The autopsy revealed classical changes of malignant nephrosclerosis, but no evidence whatever of pyelonephritis.

3. Mrs. G., age 59.—Mrs. G. made her first appearance at the Montreal General Hospital in 1942 and was seen again in 1943 for minor gynæcological treatment. On these admissions, the blood pressure was 185/100 mm. Hg, then 200/100 mm. Hg.

Six months later, in October 1943, when I first saw her, she complained of shortness of breath and severe indigestion. Her blood pressure was found to be 250/140 mm. Hg. The most striking feature was a large mass in the right side of the abdomen, which felt like an enlarged kidney. The heart, fundi, and urine were within normal limits on examination. Severe headaches developed and she became very irritable. In February 1944, when the blood pressure was found to be 260/140 mm. Hg, she was readmitted for investigation. Retrograde cystoscopy confirmed the presence of a large renal mass, with bizarre configuration of the calices and unsatisfactory urine flow on the right side. However, total renal function tests were normal. Operation (nephrectomy) was advised, which she refused chiefly because nobody would assure her that the operation would cure the hypertension.

She reappeared one year later, in August 1945, reporting that she felt miserable and lacked pep and energy. The blood pressure was found to be 260/140 mm. Hg, and there was albumin in the urine. There were early vascular changes in the fundi. Most important, the mass had increased in size. She herself had noted the enlargement.

I had no difficulty this time in persuading her that surgical treatment was urgent and life-saving. The situation was desperate; a tumour was growing larger and must be removed, whether it helped her blood pressure or not. Three days after readmission, a right nephrectomy was performed. A solid, well-encapsulated tumour, which proved to be a carcinoma, occupied the right upper pole. But the striking feature at the operation was the fact that the kidney itself had been rotated through the angle of over 45 degrees. The postoperative course was uneventful.

Since that time, eight years ago, her general condition has continued to improve. She has gained weight and strength. The fundi changes have regressed. The heart sounds have quieted down. Urinalysis revealed only a slight trace of albumin. The blood pressure has shown a gradual fall to normal levels, where it has remained.

4. Mrs. H., age 54.—Mrs. H. was referred from the outpatient department to the nose and throat service for a tonsillectomy in October 1947, but because of certain findings, instead of a tonsillectomy, a right nephrectomy was performed by Dr. Powell. Hypertension (210/120 mm. Hg) was noted and investigation revealed a mass of calcified tissue replacing the right kidney with no function and no visible ureteral orifice on that side. A preoperative diagnosis of closed renal tuberculosis was made. The pathological diagnosis read: "Old calcified caseous tuberculosis of the right kidney with almost complete replacement of the parenchyma and a marked obliterating endarteritis."

She still attends the cardiac clinic and leads a moderately active life nearly eight years after her operation. Her blood pressure recently shows a tendency to remain at a slightly elevated level of 180/88 mm. Hg.

5. (Reported by Dr. R. E. Powell in 1951.[4])—An aeroplane pilot, 32 years of age, was admitted in 1947, complaining of severe headache and pain in the right costo-vertebral angle. Hypertension (210/110 mm. Hg) had been found on routine occupational examination. He had suffered from periodic attacks of right costo-vertebral pain for the past 14 years. There were never any urinary symptoms. An appendectomy had been performed in 1941 without relief from the attacks.

Five to six months before admission, he noted the onset of severe headaches. These began in the morning and would subside towards evening. They were not influenced by flying. About this time, periodic medical examinations revealed intermittent hypertension around 160/100 mm. Hg. Two weeks before admission the headaches suddenly became more severe, and the blood pressure registered 210/110 mm. Hg. He had been working until three days previously.

He appeared healthy, but had hypertension and a mass palpable in the region of the right kidney. The heart, urine, fundi, E.C.G., and right kidney function were all normal. The retrograde pyelogram revealed a normal left kidney and a large hydronephrosis on the right side with a filling defect. A preoperative diagnosis of Goldblatt syndrome was made and right nephrectomy advised.

At operation, on December 23, 1947, a large hydronephrosis and a large aberrant renal artery causing obstruction were found and a right nephrectomy was performed.

Two days after operation, the blood pressure fell to 130/80 mm. Hg, and a routine examination regularly over a period of six years revealed a stable blood pressure around 125/80 mm. Hg. He resumed his duties as an aeroplane pilot and met his death in 1953 in the tragic T.C.A. Moose Jaw accident.

6. N.K., aged 16.—N.K. was admitted to the Montreal General Hospital on June 23, 1953, complaining of frontal headaches, dizziness, swelling of the ankles, shortness of breath and high blood pressure. Her mother, aged 53, was known to have high blood pressure. She recalled suffering from the usual sore throat, but denied any serious illnesses or operations. There was no history of nephritis or scarlet fever. When applying for a job in November 1952 (seven months before admission), she was told that her blood pressure was 190.

She was admitted to an outside hospital in December 1952. Her blood pressure readings varied from 160/200 mm. Hg systolic and 110/140 mm. Hg diastolic. The urine contained one-plus albumin with a few red blood cells. The Mosenthal test showed a fixed specific gravity at the level of 1.010. The N.P.N. was normal. The phenolsulphonphthalein test showed a diminished total renal function and, more important, a delayed appearance time of nine minutes on the right side as compared with two minutes on the left side.

The intravenous pyelogram suggested narrowing of the right ureter. She left the hospital before any final conclusions or treatment could be given. The hospital record states: "It seems reasonable to presume that this is a case of severe hypertension with organic changes, possibly on a renal basis." A further note was added that when she was seen recently as an outpatient her blood pressure was about 240/140 mm. Hg.

Investigation at the Montreal General Hospital confirmed the above findings, including the albuminuria. Coarctation of the aorta, endocrine disease, phæochromocytoma were ruled out as possible causes. A repeat intra-

venous pyelography and retrograde cystoscopy revealed abnormality of the right renal pelvis. An aortogram suggested an abnormal arterial tree to the right kidney.

The heart was not enlarged radiologically. The E.C.G. revealed no significant changes. Some observers noted slight vascular changes in the fundi. Finally, the right kidney was removed. The pathological diagnosis was hypoplastic renal artery, hypoplastic right kidney.

Postoperatively, the blood pressure fell to 120/75 mm. Hg. She is being followed up in the cardiac clinic. The urine and fundi are now normal. She is working steadily. When seen recently, her blood pressure was 130/80, two years and three months after her nephrectomy.

Unilateral functional tests including the P.S.P. and comparative urea tests indicated depressed function of the right side. Dr. Grant Reid (Urology), accepting transfer for a probable right nephrectomy, commented: "The left kidney is, I believe, somewhat sub par." The aortogram was not successful, neither renal artery being visualized. The preoperative diagnosis was of chronic pyelonephritis with considerable reduction in size of the right kidney. A right nephrectomy was performed on January 26, 1954. The pathological diagnosis was chronic rightsided pyelonephritis, the right kidney weighing 39 g.

Our fears have been substantiated: she has not done well. The blood pressure drop has been disappointing. She has lost weight and strength. Her blood pressure recently, despite the use of antihypertensive drugs, was 195/140 mm. Hg.

TABLE I.

UNILATERAL NEPHRECTOMY FOR HYPERTENSION

| Case No. Name | Pathology | Effect on blood pressure: No reduction | Reduced to normal 1 year or more | Duration and result |
|---|---|---|---|---|
| 1. Mrs. L.B. | Pyelonephritis | | 1 | 16 years, excellent |
| 2. Mr. D.J. | Pyelonephritis | | 1 | 14½ years, good, recurred |
| 3. Mrs. H.G. | Tumour with rotation | | 1 | 10 years, excellent |
| 4. Mrs. G.H. | Caseous tuberculosis | | 1 | 8 years, good, recurring |
| 5. Mr. W.B. | Aberrant renal artery | | 1 | 6 years, excellent |
| 6. Miss N.K. | Hypoplastic right renal artery and kidney | | 1 | 2¼ years, excellent |
| 7. Miss G.F. | Pyelonephritis | 1 | | 1½ years, failure |
| Total | | 1 | 6 | 4 excellent, 2 good, 1 failure. |

7. G.F., 15 years old.—G.F. was admitted to the Montreal General Hospital in January 1954, complaining of severe frontal headaches, impairment of vision and dull pain in both sides of the abdomen for almost a year. There was no history of rheumatic fever or nephritis.

She was perfectly well until about one year previously (1953), when she developed frontal headaches once or twice a week. She was told she had sinus trouble. Six months later she awakened one morning feeling strange and confused and could not see her mother in the room. Admission was arranged in another hospital on August 3, 1953. The blood pressure ranged around 280/180 mm. Hg. The E.C.G. was normal. The heart was reported enlarged, the fundal vessels abnormal, and albuminuria and hæmaturia were noted. Intravenous pyelography showed a small right kidney and deformity of the calices. She was treated with hexamethonium and Apresoline, appeared to improve, and was discharged to her local doctor. Five months later, when her symptoms were persisting and her blood pressure was found to be 190/150 mm. Hg, she was referred for further investigation.

On admission in January 1954, examination confirmed the previous findings. The blood pressure was 220/160 mm. Hg. Colour and nutrition were good. The heart was enlarged, and there was a loud grade III systolic murmur audible over the entire precordium. In the fundi there were marked vascular changes suggestive of advanced hypertension without any hæmorrhages. The electrocardiogram was normal.

Albuminuria, 30 mg. per 100 c.c., was present along with a few red cells, 8-11 white cells, but no casts.

Renal function tests revealed impairment of total kidney function: the specific gravity was fixed at around 1.005; the fractional P.S.P. excretion was diminished to 16, 10, 5 and 10% (normal value 25% in the first half hour, then 20, 15 and 10%); furthermore, the blood urea nitrogen was slightly elevated to 24 mg. % and the creatinine slightly over normal (2.1 mg. %). Retrograde pyelography confirmed that the right kidney was small.

## DISCUSSION

Table I shows a summary of the pathological conditions encountered and the results obtained. In all seven cases in this series the right kidney was diseased. Pyelonephritis occurred three times. The remaining diagnoses consisted of tumour with rotation, caseous renal tuberculosis, aberrant artery with hydronephrosis, and hypoplastic kidney and renal artery. It is thus evident that there is no single specific pathological entity. Indeed, a variety of pathological lesions is characteristic of unilateral renal hypertension.

## RESULTS

Four of the seven operations have shown excellent results, and cure is considered permanent. In two cases results are good at 9 to 14½ years after nephrectomy. Patient No. 4, with renal tuberculosis, is still alive and well, but after nine years there is now a return of the hypertension. Patient No. 2 was well and active for 14½ years, then developed a sudden recurrence of severe hypertension and died, with classical findings of malignant hypertension.

There was one failure (No. 7), with no improvement in blood pressure even temporarily. She is still alive 1½ years after nephrectomy, being treated by hypotensive drugs. Despite the delay in diagnosis, realizing her desperate state, we were anxious to give her the benefit of the doubt. In these last three cases bilateral renal disease was present to some degree before nephrectomy.

## LITERATURE

Smith,[5] in 1948, reviewed the literature critically and reported 242 cases in which unilateral nephrectomy had been performed for hypertension. Of these, he accepted 47 as possible cures on the basis that the blood pressure was reduced to 140/90 mm. Hg or less for at least one year or more, a cure rate of approximately 20%.

Thompson and Smithwick,[6] in December 1952, collected an additional 57 cases and accepted 26 of these as meeting the criteria of cure. The total number of cases thus reported is 299, with 73 of these classed as cured. This represents a cure rate for unilateral nephrectomy of 24.4%.

In 1952, Braasch[7] reviewed 100 cases in which nephrectomy had been performed for hypertension. The blood pressure returned to normal or was significantly reduced in 64% of cases followed up from two to five years, and in 53% of cases traced from five to nine years postoperatively.

Allen,[8] in 1951, stated that in hypertensive cases with unilateral renal disease, either of the main renal artery or parenchyma or both, the contralateral kidney is observed at autopsy to be altered by the vascular changes of benign nephrosclerosis. Many of the failures to relieve hypertension by excision of an abnormal kidney are very likely based on the presence of arteriolosclerosis produced in the initially normal kidney by the hypertensive state. This contralateral renal arteriolosclerosis appears to sustain the hypertension after nephrectomy, hence the need for discovering the hypertension early. The blood pressure may drop to normal after nephrectomy, and then gradually return to higher levels after an interval of several months to years.

The cause of the hypertension in unilateral renal disease is not known. Of the many theories advanced, the following three are outstanding:

1. That the kidney secretes an excess of circulating pressor substance (Houssay, Page, Wakerlin).
2. That the kidney fails to detoxify a normally existing pressor compound (Bing and Zuker).
3. That the kidney fails to produce its normal supply of humoral agent (Grollman).

Ask-Upmark[9] remarked that this disease occurs most frequently in girls, and is supposed to be due to a congenital anomaly of the *right* kidney. Perera[10] suggests that the mechanisms involved in hypertension associated with unilateral kidney disease differ from those related to certain chronic bilateral renal disorders and to hypertensive vascular disease.

## SUMMARY AND CONCLUSIONS

Our experience and that in the expanding literature would indicate that a unilateral renal lesion can cause hypertension, and furthermore that removal of the diseased kidney can cause the blood pressure to return to normal. Such cases are not common. Excluding the inoperable cases, at the Montreal General Hospital we encounter about one case a year.

A great variety of kidney lesions may give rise to the hypertension. The unilateral renal disease may be primarily parenchymal or primary vascular in origin. By far the most common single disease is pyelonephritis. The cause of the hypertension is not known, but a renal pressor mechanism can be reasonably incriminated.

The importance of thorough renal studies in all patients with hypertension cannot be overemphasized. In addition to intravenous and retrograde pyelography, we have used the air insufflation technique and more recently aortography.

Great caution must be exercised by the internist and urologist in the selection of cases for nephrectomy. To date the following general rules have been advanced. (1) The opposite kidney should be normal. (2) The hypertension should be of less than two years' standing. The duration of the hypertension has a direct relationship to the expected result. (3) Retinal changes should be minimal. (4) The renal lesion should be confined to one kidney, which should show definite loss of function. It is inadvisable to remove the poorer of the two involved kidneys. Our last patient (No. 7) illustrates this point.

Many authors have stated that the indication for radical operation should be based on uro-

logical grounds rather than on the presence of hypertension. Yet in our experience it has been the hypertension which has brought the patient to seek relief. Therefore, hypertension itself becomes important. Moreover, it often presents as malignant hypertension and may have a rather characteristic clinical picture. Hence, this pattern of disease should be borne in mind, especially in young patients.


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# PLURIGLANDULAR INSUFFICIENCY WITHOUT PANHYPOPITUITARISM*

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SYNDROMES characterized by functional impairment of several endocrine glands often arouse the physician's interest and tax his diagnostic acumen. Similar clinical states may result from insufficiency originating in any one of or in several different glands. This is due to the multiple interactions between the components of the endocrine system. Furthermore, there are many causes of the primary glandular failures, so that the etiology in the individual case is often obscure.

The case to be reported was a diagnostic problem, and remained a riddle because of the unexpected lack of response to multiple endocrine replacement therapy. This therapeutic failure, however, permitted the pathological demonstration of histologically intact, though functionally inadequate, adrenal glands in a case of primary hypothyroidism and diabetes mellitus.

## CASE REPORT

This 43-year-old French-Canadian labourer had first been seen at the Out-patient Clinic in 1945. He had gradually lost weight from 160 to 131 lb. over several years, and polyuria and polydipsia were first noted in August 1945. He also admitted chronic constipation and occasionally heartburn. The only notable physical findings in December 1945 were malnutrition and the absence of the knee and ankle jerks. His height was 67½ inches (lm. 69). The blood pressure was 116/84 mm. Hg. Blood findings were as follows: Wassermann reaction negative; sugar 333 and 344 mg. %; cholesterol 244 mg. %; non-protein nitrogen 17 mg. %. In January 1946 the diabetes was under fair control with diet and 40 units of protamine zinc insulin each morning.

Shortly thereafter, he stopped taking insulin without medical advice because of morning faintness and decreased appetite. Increasing weakness, pains in the legs, and diminished vision followed. In June 1948 the downhill course was accelerated by a subcutaneous infection in a finger, which was resistant to treatment but finally responded to penicillin therapy during September. The next month he returned to the Diabetic Clinic and was admitted to hospital on October 1 (No. 6854-48).

Additional history was the absence of libido or ejaculations for two years. A slow manner of speaking and moving was obvious and he frequently fell asleep when not disturbed. The pulse rate was 80, blood pressure 110/80, and weight 133 pounds. He spoke in a deep guttural voice. The skin was pale, dry and cool. The hair was dry and of male distribution, but was quite sparse in axillary and pubic areas. There was puffiness of the periorbital tissues. The pupils were small and reacted sluggishly to light. The ocular fundi and visual fields were normal, but there were bilateral immature cataracts. The tongue was large. The thyroid gland was not palpable. The heart, lungs, and abdomen were normal. The phallus and testes were of normal adult size, but the prostate was atrophic. Arterial pulsations in the feet were absent. The abdominal and plantar reflexes were normal and vibration sense was present. Knee and ankle jerks were absent.

*Initial diagnosis.*— Diabetes mellitus and hypothyroidism. The possibility of hypopituitarism was suggested.

*Laboratory findings.*—Urinalyses: Specific gravity 1.012 to 1.022; sugar 0 to 4 plus; albumin 0; acetone 0; microscopically, no cells or casts. Hæmatology: white cell count 8,000; hæmoglobin value 76%. The serum Wassermann and Kahn tests were negative. Gastric analysis showed free hydrochloric acid. Three determinations of the basal metabolic rate were between minus 22 and minus 27 before therapy. Plasma cholesterol readings were 163 and 134 mg. %. Fasting blood sugar was initially 384 mg. %, but after insulin therapy values between 73 and 140 mg. % were obtained. Serum bilirubin was 0.1 mg. %. Blood urea nitrogen was 13 mg. %. Serum phosphorus was 3.5 mg. %. Urinary gonadotropins by the method of Klinefelter, Albright and Griswold[1] on October 16 were greater than 6.5 but less than 13 mouse units per 24 hours, which is within the normal range. Urinary 17-ketosteroids were 7.0 mg. per day.

Radiography showed clear lung fields and a cardiacthoracic ratio of 14.8/30.0 in cm. The sella turcica was normal. Calcification was noted in the right peroneal artery. Electrocardiogram showed a rate of 82 per

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†Oklahoma Medical Research Foundation, Oklahoma City, Okla.

minute, low and slurred QRS complexes in leads 1, 2, and 3, flat T wave in lead 1, and a relatively low T wave in lead V 6.

*Treatment.*—After slightly greater amounts of insulin initially, control of hyperglycæmia and glycosuria was obtained with 20 units of globin insulin before breakfast and 10 units of protamine zinc insulin before supper daily and a high carbohydrate, 1982-calorie, diabetic diet. Thyroid extract was begun on October 18, 1948, at one-half grain daily and increased at weekly intervals to three grains daily.

*Clinical course.*—Diabetic control remained good. While he was on thyroid therapy, pulse rates varied between 92 and 108, three basal metabolic rate determinations were between minus 14 and minus 21, and plasma cholesterol ranged from 145 to 94 mg. %. On October 27, plasma chloride was 84 mEq. and serum sodium 120 mEq. per litre. He was afebrile. Without evidencing appreciable change in symptoms and weighing 133 lb., he was dicharged to the Montreal Convalescent Hospital on November 20.

*Interval history.*—Lassitude, diurnal sleepiness, weakness of legs, and anorexia continued despite insulin, thyroid and vitamin therapy. Skin ulcers appeared over the right triceps, left buttock and base of the coccyx. A 24-hour specimen of urine collected on November 26, 1948, contained 17-ketosteroids 4.3 mg., biologically active corticoids 18 glycogen units,[2, 3] and periodic acid reacting corticoids 0.355 mg.[4] All these results were below normal.

*Second admission.*—On December 9, 1948, he was readmitted. The pulse was 112 per minute, weak, and thready. The blood pressure was 80/65. There was no pitting œdema or congestion. Ulcers on the skin were present as indicated above, but otherwise the results of physical examination differed little from those of the previous admission.

*Clinical impression.*—The lack of response to thyroid therapy and the increasing evidence of adrenal insufficiency cast doubt on the diagnosis of simple hypothyroidism and supported a diagnosis of panhypopituitarism. Other observers, cognizant of the normal gonadotropin secretion, favoured simultaneous adrenal and thyroid insufficiency.

*Laboratory investigation.*—Urinalyses were negative except for the presence of glucose occasionally. Hæmatological reports showed anæmia. There were 693 and 291 eosinophils in stained smears. Blood urea nitrogen and sugar and serum bilirubin values were not remarkable. During the first week of this admission, the patient was on three grains of thyroid daily, and the B.M.R. was minus 10, serum cholesterol 111 mg. %, serum sodium 120 mEq. per litre and serum chloride 90 mEq. per litre. Urinary 17-ketosteroids were 5.0 mg. and gonadotropins[1] were greater than 26 mouse units per 24 hours. The patient was unable to co-operate in repeated attempts to use the Robinson-Kepler-Power water load test.

*Treatment.*—On December 18, 1948, thyroid therapy was stopped and adrenocortical replacement therapy instituted. Because of the scarcity of cortisone and the presence of diabetes, sodium chloride was given by mouth and desoxycorticosterone actetate intramuscularly. Aqueous cortical extract, 50 c.c. intravenously, was given on January 10, 1949, during the excision of the margins of the decubitus ulcer. Doses of desoxycorticosterone were gradually reduced to 2.5 mg. daily on January 14, and maintained at near this level to February 22. He also received vitamin therapy, a course of streptomycin therapy, and three courses of sulfadiazine therapy during these two months, and insulin daily. Laboratory investigations during this period included an intramuscular ACTH test using 21 mg. of the Armour standard preparation. Circulating eosinophils were 631 before and 595 per cu. mm. after the injection. Changes of approximately 10% occurred in the excretion of uric acid, chloride, potassium and 17-ketosteroids and there was a rise of only 24% in the periodic acid reacting corticoids. The normal change should be 50 to 100% or more for these indices. While the patient was off thyroid therapy, a B.M.R. of minus 27 and a serum cholesterol of 154 mg. % were recorded. Treatment with one grain of thyroid extract was resumed from January 26 to February 22, and on February 8 the B.M.R. was reported as minus 1. X-ray films of the lungs, lumbar spine, sacrum and skull were normal.

*Clinical course.*—The patient weighed 109 lb. on December 13, 121 lb. on January 11, and 128 lb. on February 8. The weight gain was attributed to salt and water retention. Increasing lassitude, occasional bouts of diarrhœa, chelosis, the deterioration of the sacral ulcer and the appearance of a new skin ulcer on the right thigh were noted. This unfavourable progress prompted the decision on February 23 to discontinue all therapy except insulin and to observe the results. The downhill course continued. The heart sounds became so distant that pericardial effusion was suspected but not confirmed. Low-grade fever and pulmonary rales were present. The blood showed Hb 8.7 g. % and 9,700 white cells with 90% polymorphonuclears. Treatment with aqueous cortical extract intramuscularly was begun on March 3.

The ulcer on the right thigh progressed in extent and depth to a stage of gangrenous necrosis. Blood cultures showed no growth. Penicillin therapy was resumed, and a wide surgical excision of the gangrenous area was performed on March 6. Although organisms resembling clostridia were seen on smears, cultures of the aspirated fluid revealed predominantly anaerobic streptococci. He died on March 8, 1949.

## AUTOPSY

The post-mortem examination was made four hours after death. The body was that of a well-developed, somewhat cachectic adult white male measuring 160 cm. in length. The hair was black and balding at the temples. There was a draining decubitus ulcer measuring 5 x 3 cm. over the lower sacrum with a large surrounding area of induration. There was a small para-anal ulcer. On the posterior aspect of the right thigh was an oval defect which measured 27 x 15 cm. The floor of this defect was pea-green in colour and consisted of the posterior muscles and deep fascia. Necrotic softening was evident.

There was about 75 c.c. of clear fluid in each pleural cavity and only 15 c.c. of straw-coloured fluid in the pericardial cavity. Heart's blood culture failed to reveal bacterial growth. The heart weighed 425 g., and was without gross lesions. The coronary arteries and the aorta appeared normal and showed little or no arteriosclerosis. The right lung weighed 490 g. and the left 400 g. The pleuræ were smooth. There were no areas of induration but minimal pulmonary œdema was present.

The peritoneal cavity contained about 1,000 c.c. of clear greenish fluid, but the peritoneum was smooth and glistening. The organs of the gastrointestinal system were grossly normal. The liver weighed 1,600 g. and the pancreas 80 g.

The kidneys each weighed 200 g. Except for a minute white area in one renal cortex, the kidneys, bladder, prostate and testes appeared normal. The spleen weighed 230 g. and was firmer than usual. The bone marrow appeared normal. There were small discrete lymph nodes in both axillary and inguinal regions. The cranial contents appeared normal, the brain weighing 1,415 g. The arteries comprising the circle of Willis had very little sclerosis.

*Gross examination of the endocrine glands.*—The thyroid gland weighed 11 g. It was pale yellow in colour, very firm in consistency and of the usual configuration. On serial section the gland appeared to consist wholly of firm, white homogeneous tissue, resembling fibrous tissue. Parathyroid glands were not recognized. The right and left adrenal glands weighed 8 and 10 g. respectively, and were normal in position and appearance. On section the cortex was firm, yellow and thin, the medulla softer and brownish. Neither adrenal gland showed gross evidence of disease. The pituitary gland was normal in size, shape, and position, and it showed no gross abnormality on external examination or section. The testes and pancreas were grossly normal.

## MICROSCOPIC EXAMINATION

The wound edge showed massive suppuration and associated venous thrombosis. Cultures of this area, both ante-mortem and post-mortem, yielded anaerobic streptococci, bacteroides and staphylococci but not clostridia. There was an acute exudative interstitial hepatitis and a small focal necrosis, presumably an infarct, in the left kidney. Mild pulmonary congestion with occasional areas of peribronchial fibrinous pneumonia were also present. Otherwise the abnormalities were confined to the endocrine system.

## MICROSCOPIC EXAMINATION OF THE ENDOCRINE GLANDS

*Thyroid.*—The tissue is barely recognizable as thyroid gland, consisting mainly of fibrous connective tissue with larger and smaller blood vessels closely aggregated. This condensation of stroma is the result of widespread atrophy and loss of the glandular parenchyma, of which there remain minute islands consisting of markedly shrunken and atrophied acinar elements (Fig. 1). An occasional acinus contains a small amount of fragmented colloid which stains abnormally. A few scattered lymphoid cells are present between these shrunken acinar elements and at a few points are aggregated into small nodular foci. One small lobule remains in which a number of acini are better preserved and are distended by colloid of a more normal appearance. The blood vessels are not abnormal. The gland is enclosed by a loose fibro-fatty tissue. The process appears to be one of simple parenchymal atrophy with condensation of the stroma, and not a true productive fibrosis or inflammatory lesion.

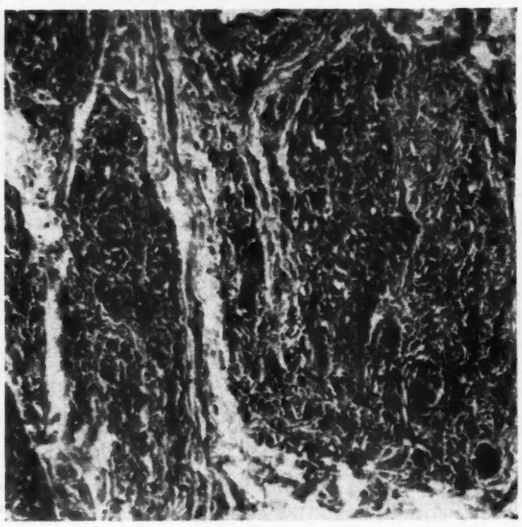

Fig. 1

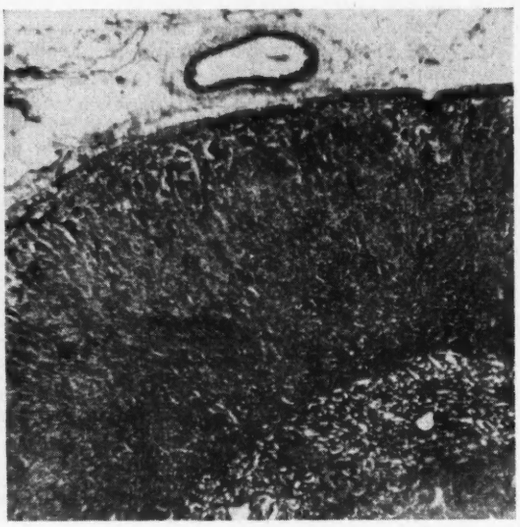

Fig. 2

Fig. 1.—Thyroid × 100. Note the scanty shrunken acini in a collapsed fibrous stroma.
Fig. 2.—Adrenal × 35. Note the preserved cortex and medulla without gross structural change.

*Adrenal glands.*—The appearance of the right and the left adrenal is similar. There is a thin intact capsule and an apparently normal cortical structure with the three anatomical zones distinct (Fig. 2.) No evidence of atrophy, necrosis, fibrosis or an inflammatory lesion is found. The cortex appears to be well preserved, and staining of frozen sections with Scharlach R reveals an abundant content of lipoid (Fig. 3.) The medullary tissue is well preserved and shows no lesion. In sections fixed with bichromate solution and stained with toluidine blue (Wiesel's method) the medullary cells have a green cytoplasm, indicative of an abundance of chromaffinic material. The glandular, capsular and periadrenal blood vessels appear normal. Adrenal tissue was also submitted to Dr. C. P. Leblond, who reported no apparent abnormality of the cortex in sections stained with fuchsin sulphurous acid.

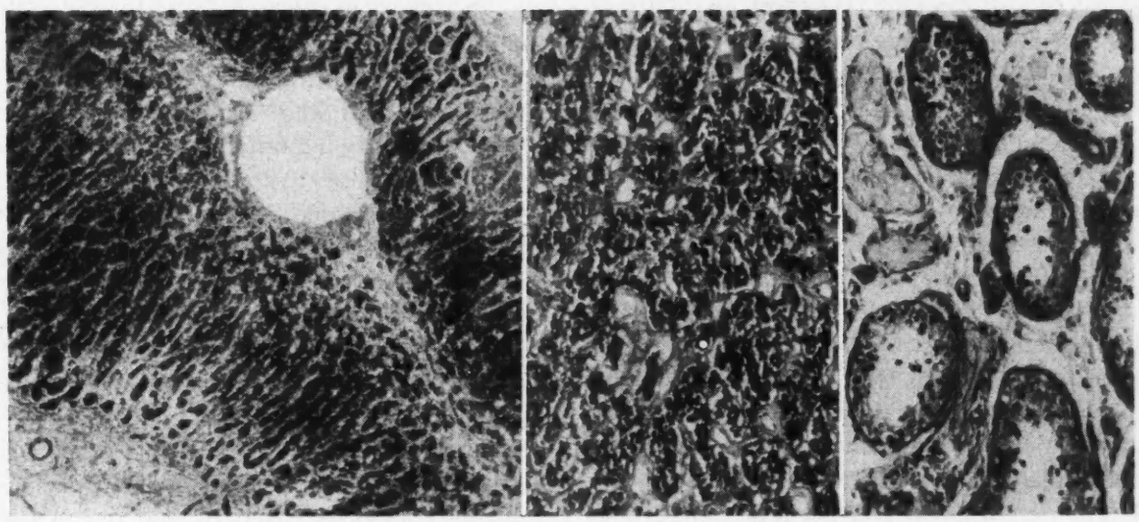

Fig. 3. Fig. 4 Fig. 5

Fig. 3.—Adrenal × 35, frozen section with Scharlach R staining. The dark material in the photograph represents abundant cortical lipoid material. Fig. 4.—Pituitary × 100. There is a normal arrangement of acini and stroma in pars anterior. Fig. 5.—Testis × 100. Note the few shrunken, atrophic and hyalinized tubules amongst a vast predominance of preserved ones.

*Pituitary gland.*—The section includes only the pars anterior (Fig. 4). It has an essentially normal architecture with the exception that the interstitial tissues are prominent and there is an apparent increase of the fibrous stroma. This probably is evidence of a mild degree of parenchymal atrophy. The parenchyma has its normal cellular components, containing a few scattered calcaroid bodies. No inflammatory or vascular lesion is evident.

*Testes.*—The tunica albuginea of the right testis is of normal thickness and appearance. There is no abnormality in the number of the interstitial cells of Leydig and these appear normal. The seminiferous tubules are diffusely depleted of their spermatogenic epithelium and relatively few spermatogenic cells remain. The Sertoli cells are retained and the tubular basement membranes are thin and intact. No inflammatory or fibrotic lesion is present. The left testis is generally similar to the right but retains a slightly greater amount of spermatogenic epithelium. In some tubules a few spermatids are formed but no mature spermatozoa. In one or two small foci, several tubules are totally atrophied and hyalinized (Fig. 5). No other lesion is evident.

*Pancreas.*—The gland has a normal structure and reveals no atrophy, fibrosis or inflammatory process. The islets are of normal size and reveal no degeneration, atrophy or hyalinization.

## SUMMARY OF PATHOLOGICAL FINDINGS

The principal abnormality in the endocrine glands was the severe parenchymal atrophy of the thyroid gland. No lesion of the adrenal glands was evident and there was only a minor degree of parenchymal atrophy of the pars anterior of the pituitary gland. There was a moderate degree of hypospermatogenesis but the interstitial cells of Leydig in the testes were normal. The pancreas appeared normal but this is not uncommon in diabetes mellitus. Additional findings were the marked cachexia, sacral decu-

bitus ulcer, gangrenous necrosis of the posterior surface of the right thigh, acute exudative interstitial hepatitis, focal cortical necrosis of the kidney, congestive splenomegaly, mild pulmonary congestion, organizing peribronchial fibrinous pneumonia, bilateral pleural effusion and peritoneal effusion.

## DISCUSSION

The case will be discussed first from the viewpoint of physicians who studied the clinical course and later from the retrospective aspect of a knowledge of the post-mortem findings.

One of the first suggested clinical diagnoses was panhypopituitarism. Points favouring this, rather than primary hypothyroidism, were first the cachexia and the failure to find elevated serum cholesterol values, and later the mounting evidence of adrenocortical hypofunction despite thyroid therapy. However, there were many cogent reasons against the diagnosis of panhypopituitarism. The testes were of normal size and consistency, and normal quantities of urinary gonadotropins were detected on two occasions, so one must conclude that this function of the pituitary was normal. Furthermore, there was moderate amount of urinary 17-ketosteroids (7.0, 4.3, and 5.0 mg. per day) on three occasions before adrenal therapy. Ketosteroids may be of gonadal or adrenal origin, but in any event some pituitary tropic hormone secretion is required for their production. Other points against hypopituitarism were the absence of visual field impairment or of roentgenographic evidence of enlargement of the sella turcica. These last are actually points against an expanding pituitary tumour, but such is the cause of pituitary failure in the vast majority of adult men, whereas postpartum pituitary necrosis is a common cause in women. Additional but less clear evidence against panhypopituitarism in the present case was the absence of response to the intramuscular test dose of ACTH. Such a negative response might be present in cases of hypopituitarism with long-standing adrenal atrophy and yet these cases should show normal responses to single or repeated intravenous administrations of ACTH.[5, 6] A final bit of evidence against hypopituitarism, and incidentally against hypoadrenalism of any type, was the fact that this patient had fasting blood sugar levels between 143 and 344 mg. % and never manifested hypoglycæmia during hospitalization, although he received total daily amounts of 30 to 50 units of insulin from October to December 1945, and 10 to 20 units from January to March 1949. The response to the tolerance test with intravenously administered insulin was never determined because of the obvious presence of diabetes mellitus. Bernstein[7] presented rather similar considerations in discussing a case in which hypopituitarism was suggested. The conclusion after post-mortem examination in his case was that the sequence had been first diabetes mellitus, then adrenal insufficiency due to cytotoxic dissolution of the adrenals with consequent improvement in the diabetes, and later the onset of primary hypothyroidism. Finally, before the possibility of hypopituitarism in our case is entirely excluded, it must be recalled that pituitary deficiency is not always "pan"—that is, complete. Sheehan and Summers[8] noted a number of cases with organic lesions involving the pituitary gland in which certain aspects of the syndrome developed slowly or even failed to appear, and this point has been recently presented again.[9]

Since panhypopituitarism in our case seemed unlikely, primary hypothyroidism was the favoured diagnosis during the first admission. The fact that evidence of adrenal hypofunction might be found in hypothyroidism was known. Talbot and co-workers[10] had reported low urinary 17-ketosteroid levels, and subsequently Talbot and others[11] also noted low urinary reducing steroid levels in cases of myxœdema. However, these authors noted a prompt rise of the urinary corticoids to normal with thyroid therapy. In our case such a response did not occur; instead hyponatræmia developed, with increasing clinical evidence of adrenal insufficiency during the first two months' trial of thyroid therapy.

For these reasons the combination of organic lesions in the thyroid and adrenal glands was suspected. Such a case was first reported by Schmidt[12] and more recently the syndrome has been presented and reviewed by Bloodworth, Kirkendall and Carr.[13] This syndrome must be distinguished from that in which the pituitary gland is also fibrosed or atrophied.[14]

While our patient was off thyroid therapy, the excessive chloride excretion, eosinophilia, hyponatræmia and absence of response to the test dose of ACTH indicated adrenal hypofunction. Incorrectly, during the final stages of his illness, it was assumed that the adrenal insufficiency

was of a primary type rather than due to hypothyroidism. However, it is now appreciated that, if the adrenal cortex could not respond to endogenous ACTH because of the absence of thyroid hormone, one could not expect it to respond to exogenously administered ACTH.

The later reports of Statland and Lerman[15] and of Paull and Phillips[16] have demonstrated the clinical course of functional hypoadrenalism in cases of hypothyroidism. In the case reported by the latter authors, the signs of adrenal hypofunction persisted until thyroid and adrenal therapy had been given together for four months. Therefore, it is now comprehensible why adrenal function in our patient remained deficient during the first course of two months of thyroid therapy and during the second period of 28 days of combined thyroid and desoxycorticosterone acetate therapy. Whether or not the inadequacy of thyroid and adrenal therapy was of major consequence in the patient's death is not clear, since the progressive necrosis of the skin ulcers with the consequent reactions in vital parenchymatous organs was probably more closely related to the diabetes mellitus with its associated impairment of the neurological and vascular systems.

*Comments on the pathological findings.*—The evidences of severe chronic infection in a case of clinically established diabetes mellitus merit no further comment. Of the endocrine glands, only the thyroid showed a significant abnormality. The severe parenchymal atrophy of the thyroid was associated with an increase in stroma but this was believed due to the loss of glandular tissue rather than to an inflammatory fibrotic process. Since the pituitary and other endocrine glands were essentially normal, we have concluded that the thyroid atrophy was a primary condition.

In recent years, however, there has been an increasing appreciation of clinical syndromes manifested by deficiencies of single tropic hormones of the anterior pituitary gland.[17] Eunuchoidism in the male or amenorrhœa associated with decreased excretion of gonadotropins without other secondary or localized signs indicating a pituitary disorder is not uncommonly seen. Maddock and his associates[18] have reported four cases, all in males, which in the clinical and laboratory studies indicated a selective pituitary failure characterized by deficient adrenocorticotropin and gonadotropin secretion with intact thyrotropin secretion.

Most relevant to the present case is the report by Shuman[19] of a female diabetic patient with definite hypothyroidism and with normal adrenal function and gonadotropin excretion. Treatment with thyroid stimulating hormone was followed by a dramatic increase in the thyroid uptake of a tracer dose of radioactive iodine $I^{131}$, so that a selective thyrotropin deficiency of the pituitary gland was apparently present. Other possible examples of selective thyrotropin deficiency are Case 9 reported by Querido and Stanbury,[20] and Case W.B. reported by Perloff and associates.[21] Since such cases have not to our knowledge come to autopsy, the histological appearance of the pituitary and thyroid glands is unknown. One might expect to find abnormalities of the basophil cells in the anterior pituitary,[22] and only a moderate atrophy of the thyroid parenchyma.[23] In our case the pituitary gland was not studied by the Gömöri stain technique,[22] but it showed no cytological abnormalities to routine stains, and the thyroid gland was severely atrophied. Although extreme degrees of thyroid atrophy have been noted in association with severe destructive lesions of the pituitary of long duration[8, 24, 25, 26, 27, 28] it seems quite unlikely that a selective thyrotropin deficiency was the etiological factor in the present case.

Seminiferous tubular atrophy with incomplete spermatogenesis as noted in our case is frequently found in chronic illnesses of any type, for example, pneumonia.[9] The characteristic testicular lesions in hypopituitarism are the degeneration or absence of the interstitial cells, and in advanced cases the disappearance of all germinal elements accompanied by lipoid accumulations in the sustentacular cells of Sertoli,[30] but such were not found in our case. We are unable to deduce whether the slight hypospermatogenesis was due to the lack of thyroid hormone itself or to the chronic general metabolic disorder related to the diabetes and widespread infections, but the latter explanation is certainly adequate.

Of greatest interest was the normal appearance of the adrenal glands on gross and microscopic examination. Primary adrenal disease and secondary atrophy following pituitary adrenocorticotropic deficiency are clearly

excluded. The clinical evidence of adrenal insufficiency and the failure of our patient to respond to the intramuscular injection of ACTH must therefore be ascribed to an absolute or relative lack of thyroid hormone. Although reversible adrenal insufficiency in cases of hypothyroidism has been reported[11, 15, 16] and discussed above, this is the first case to our knowledge in wnich a number of clinical tests of adrenocortical function were performed, and the adrenal glands were also studied by histological techniques. The observed normal structure gives a firm foundation for the clinical reports of a reversible impairment of adrenal function in primary thyroid deficiency.

In conclusion, one should remember the earlier warnings of Means, Hertz and Lerman[31] and more recently of Perkins and Rynearson[32] that evidences of impairment of the pituitary and/or adrenal glands should be sought in all cases of hypothyroidism before thyroid therapy is initiated. Secondly, if adrenal deficiency complicates primary hypothyroidism, treatment with cortisone or other adrenal steroids may be necessary together with adequate thyroid therapy for many months before adrenocortical replacement therapy may be omitted.

## SUMMARY

1. An adult male with diabetes mellitus developed hypothyroidism and clinical and laboratory signs of adrenocortical hypofunction.

2. Despite thyroid treatment the adrenal insufficiency persisted.

3. Death followed progressive weakness and gangrenous necrosis of the subcutaneous tissues.

4. Post-mortem examination revealed severe parenchymal atrophy of the thyroid gland, normal adrenal glands, a normal anterior pituitary gland except for a slight increase in its fibrous stroma, a normal pancreas, and moderately reduced spermatogenesis in the testicular tubules.

5. The differential diagnosis is discussed, first with reference to the clinical evidence and then to the post-mortem findings.

6. It is believed that this is the first pathological demonstration of structurally intact adrenal glands in a case of primary hypothyroidism with clinical and laboratory evidence of adrenocortical insufficiency.

The authors wish to acknowledge the co-operation of Drs. J. S. L. Browne, Eleanor Venning, M. M. Hoffman and H. McIntosh of the McGill University Clinical Laboratories at the Royal Victoria Hospital for conducting various of the adrenal function studies, and to thank Dr. C. P. Leblond and his associates in the Department of Histology, McGill University, for special studies of the adrenal glands. Thanks are also due to Dr. B. L. Bailey for his assistance in the preparation of the manuscript.

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## ANALGESIC EFFECT OF NISENTIL IN UROLOGICAL PROCEDURES

Nisentil (dl-alpha (1,3-dimethyl-4-phenyl-4-propionoxy)-piperidine hydrochloride) is recommended as an analgesic for cystoscopy and other urological manipulations. It was given intravenously in 30 mg. doses to 80 patients and gave satisfactory results in 76. It acts almost at once, so that cystoscopy need not be delayed, and most patients can leave the office within 30 minutes of the procedure. No untoward reactions were observed. —H. A. Garnes, *J. Urol.*, 74: 567, 1955.

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# CANCER OF THE MOUTH*

## SOME THERAPEUTIC PROCEDURES

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IN THE TWO YEARS since the inception of the Head and Neck Tumour Clinic at the Victoria General Hospital, we have seen 515 new cases of which approximately 265 were malignant tumours of the oral cavity. We shall touch only on particular facets of this subject in which we are being guided by our own experience. Obviously, any statistical conclusions of results, over so short a time, would be without value.

Our cases are, on the average, moderately advanced. The patient with a lip lesion usually presents himself early. Whether it be a reflection on man's vanity or on his powers of observation, once the growth is inside the mouth and out of ordinary sight, it seems to be out of mind as well, and the patient seeks advice much later. The rapidity of growth of an intraoral malignancy is almost unbelievable until intimately observed. We have had a nursing supervisor tell us that the carcinoma of her cheek, extending on to gingival margins above and below, appeared only three weeks before. We have watched patients, with treatment delayed because of chest disease, and seen their tumours grow almost visibly. Cancer of the floor of the mouth grows as much in a day as a cancer of the breast in a week; as much in a week as the breast tumour in two months.

It follows that the first step in good therapy is early diagnosis, and that any lesion of the mouth about which there is the least doubt must be subjected to immediate biopsy and never to the therapeutic test of salves or mouth washes.

Speaking broadly, complete surgical excision offers the best hope of cure. There are a few exceptions. The early lesion of the lip responds as well to radiation, either in the form of x-ray or radium, and the cosmetic result is usually better. However, if there be extensive destruction of tissue, surgical excision with plastic repair is best. The early lesion of the tongue may be destroyed by radium without deformity, whereas sufficiently wide excision may result in lingual disability.

For the early, minute cancer we use excision biopsy, followed by radiation to the scar in the identical dose as would be given if the lesion were still present.

We believe that the practice of first treating the extensive lesion with radiation to reduce its size, and then excising it when shrunk to operative proportions, is unsound. Such surgery cannot be curative, and postoperative results of operations on heavily irradiated tissue are sometimes disastrous. For the lesion which at operation proves to be more extensive than examinations showed, and where excision must be done with only narrow margins of healthy tissue, postoperative radiation has a place. For the lesion where radiation is the treatment of choice and radionecrosis results, post-radiation surgery is employed.

Only in these instances should radiation and operative therapy be combined in attacking the local lesion. There our dogmatism ends. There should never be a clinic rule for the treatment of any specific type of malignant oral lesion. Each patient must be presented for consultation to the surgical and radiotherapeutical staffs, both of whom should be broadminded enough in their clinical judgment to understand the limitations as well as the scope of their respective fields.

While the epithelial tumour in the mouth responds well to radiation, its metastases in the lymphatics of the neck do not. This is because of the practical problem of reaching them all with sufficient radiation. Excision is the treatment, and two questions arise. (1) Should routine neck dissections be done without palpable evidence of lymphatic involvement? (2) Is a radical neck dissection, which leaves intact the mandible and floor of the mouth, worth doing? Opinions on the first problem are divided. Dr. Hayes Martin[2] has stated that in a large series only one case of lip lesions in 16 and one of tongue lesions in five showed metastases. On this basis, and considering the magnitude of the operation, he concluded that neck lymph nodes should ordinarily be dissected only when metastases are present. In our immature series we have had the experience of finding beneath the sternomastoid malignant lymph nodes which could not be palpated even with the skin flaps reflected, and of finding many nodes involved where we suspected only one. Despite such instances, we do follow this more conservative

*From the Departments of Surgery and Medicine, Victoria General Hospital and Dalhousie University, Halifax, N.S. Presented at the Section of Surgery, Conjoint Annual Meeting of the British, Canadian and Ontario Medical Associations, Toronto, June 21, 1955.

course; but when satisfactory removal of the local lesion requires hemi-mandibulectomy we then do a radical neck dissection routinely as part of the operation. There can be no question that, if the neck is to be opened, nothing less than a radical operation is justifiable. In some of our earlier cases, fearing the risk, we carried out modified procedures, only to have them return within months showing metastases below the operative area.

The second problem, whether neck dissection is of value unless the floor of the mouth and adjacent section of the mandible be also removed, is based on the mode of malignant spread from mouth to neck. Is it by embolic cells, or by invasion of the lymphatics? The embolic cell is commonly blamed. Our own studies are inconclusive, but in isolated cases we have shown definite invasion of the lymphatics. In one instance the involved channels passed through the mandible to the submandibular lymph nodes. However, such single findings prove nothing, and again we have compromised by removing the mandible when removal was indicated by the nature of the primary lesion and, in the other cases, doing the radical neck dissection down to bare bone and deep into the floor of the mouth, presumably leaving lymphatic channels from that point to the site of the tumour. We are not happy about this.

In doing this radical surgery on old men, and most of our patients are old men, we have been repeatedly amazed at the way they have stood the operative procedure, at their recuperative powers and their good psychic adjustment to the mental and physical upheaval in their hitherto stable lives. The assessment of the operative risk to these patients is based, not on electrocardiograms, laboratory findings or the opinions of consultant specialists, but on the clinical judgment of us who are constantly among them. On our clinic room board we have posted the saying of Jules Abel: "There is no medical contraindication to cancer surgery."

The radical operation is done through a "Y-on-legs" incision; the resection begins at the clavicle, severing the sternomastoid and jugular vein, and sweeping up *en bloc*. Spinal accessory and cervical nerves are preserved, if this can be done without jeopardizing the completeness of the dissection. Much more important to save is the lower branch of the facial, as it loops below the mandible. The patient will have deformity enough without the addition of paralysis of the corner of his mouth. This nerve can most readily be found crossing the facial vein as the vein passes beneath the parotid. A tracheostomy is done routinely, and always through a separate incision, since we learned that the unavoidable infection about the tube would spread up into the operative area if given opportunity.

Postoperative feeding has been a problem. Most patients have no desire to eat. Eating is too painful, and it is best that they do not eat because of stress put on the intraoral incision. It is impossible to supply their food needs intravenously and there is the ever-present risk of overtaxing the aged patient with water and electrolytes. The gastrostomy, as used in some clinics, seems to us radical, adding another major operation to an already overburdened patient. Conventional feeding through the intranasal rubber tube is unsatisfactory for many reasons. The plastic gastric tube seems to offer the solution. Mucosal irritation seldom occurs, and the tube is well tolerated even when left in place for many weeks.

On the evening before operation a polyethylene tube, of 2.08 mm. diam., is passed through one nostril into the cardiac end of the stomach and 1,000 ml. of 5% glucose in water is given slowly during the night. Before operation the tube is filled with water and sealed to prevent plugging.

The patient receives 2,000 ml. of 5% glucose in water intravenously during the operation and while in the recovery room—his only intravenous feeding. Six hours postoperatively, the tube is opened and a feeding of 5% glucose in water is begun (very slowly). If tolerated, this is increased to 10% glucose in water. The following morning other feedings are added.

On the first postoperative day (March 7), the patient whose chart appears (Fig. 1) received 150 g. of carbohydrate, 35 g. of fat, and 80 g. of protein. Total calories were approximately 1,200. Quantities were increased slowly and minute token doses of oral fluids given. At one week oral feedings were increased sharply and tolerated, and the tube was removed. Nitrogen intake on March 7 was 12 g.; urinary nitrogen, 5 g. Chart and clinical observation showed that a reasonable balance was maintained throughout. Creatinine level was constant. Serum calcium, phosphorus and protein levels rose during the week.

In general, solutions for enteral feeding must be relatively sterile, stable, and of such viscosity that they can be administered through a tube. They should not produce gastrointestinal disturbance and must have an adequate nutritive value.[2-5] When these requirements are met, the technique of administration becomes important because a volume greater than 3,000 ml. in 24 hours may produce nausea, vomiting and diarrhœa, and rapid delivery will cause the same symptoms. An apparatus has been devised to help to control conventional drip feedings. The apparatus described is physiological in its function in that it mimics the mechanics of deglutition. Hydraulic flow of food, once set, is automatic, but still subject to physiological control. Thus, increased intragastric pressure, whether from distension, hyperactive peristalsis, or even from coughing or talking, checks its flow.

We are using some intraoral appliances in the rehabilitation of these patients, but have as yet no experience in the use of interstitial mandib-

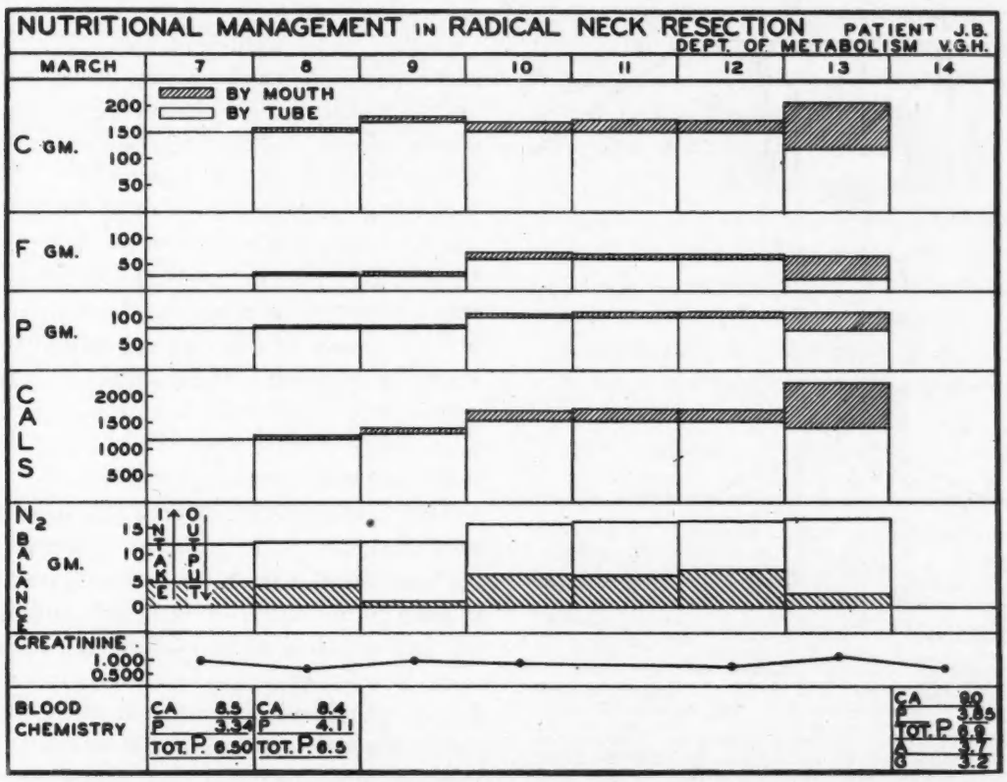


Fig. 1.—This patient (who had a radical neck dissection with hemi-mandibulectomy and resection of the cheek) received, via the gastric tube, milk, tea, strained soup, 10% glucose in water, and 15% "egg albumin" (albumin, globulin, lipoprotein) to which the required vitamins, choline, glucose and sodium alginate had been added.

answer this demand (Fig. 2). With it, these feedings can be administered: aqueous solutions (coffee, tea, glucose, sucrose), strained fruit juices, soups, milk, most commercially prepared tube feedings and specially prepared egg albumin, custard, liver, beef, fish and vegetable tube feedings.

We believe that the patient who has had an operation which prevents his eating normally, or whose ability to eat is impaired by any critical illness, should be given food from natural sources which he can assimilate. He should not be totally dependent on commercially prepared feedings, or at the mercy of often inexperienced ular replacements. The ideal appliance should lend itself to insertion at the time of operation, because the life expectancy of these patients is not great. They have not the time for secondary, plastic repairs. It must be readily inserted, so as not to prolong an already arduous operation, and it must be completely non-irritating to allow for healing. Published results in the use of these appliances show them about 50% satisfactory, and our own work in this field is only speculative and experimental.

Even with the therapeutic improvements of recent years the greatest hope in oral cancer lies in prophylaxis. This means good food, good

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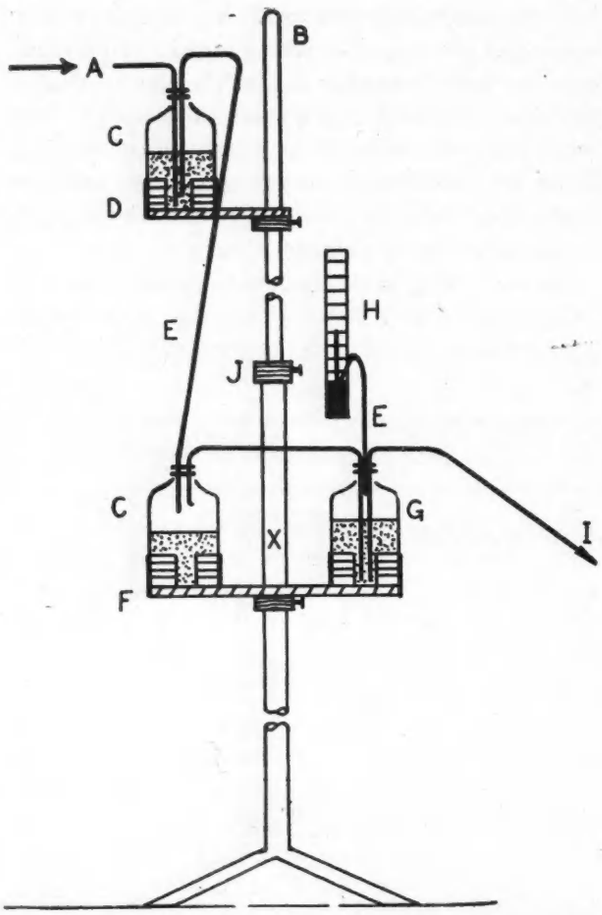


Fig. 2.—An apparatus for enteral feeding or intravenous therapy.

(A) Air inlet. (B) Adjustable stand. (C) 500 c.c. or 1,000 c.c. glass bottles for $H_2O$. (D) Single movable platform. (E) Polyethylene tubing. (F) Double movable platform. (G) 500 c.c. (or small plastic) bottle for food or intravenous solution. (H) Manometer, to be clamped on stand at X. (I) Gastric tube (to stomach) or intravenous tube with needle (to vein). (J) Adjustment for stand.

*Method of operation.*—(1) Fill bottle C (top) with 1,000 c.c. or 500 c.c. water, as required. (2) Attach bottle G (tube feeding or intravenous solution) to the system. (3) Adjust the manometer to proper reading. (4) Inject 10-20 c.c. air into air inlet (A), to initiate the flow of $H_2O$ from C (top) to C (bottom). (5) The rate of flow is governed by the distance between bottles C and the distance between F and the outlet of the gastric tube or intravenous needle. (6) If the manometer reading continues to rise, it is indicative of occlusion of the gastric or intravenous tube or of increased gastric pressure. On the other hand, if the reading continues to fall, there is difficulty in the proximal section of the apparatus, i.e., before reaching bottle G. (7) When bottle (C top) is nearly empty, exchange it with the lower bottle (C). (8) A screw clamp can be used on tube (E) for better control of flow. (9) Manometer (H) is not a necessity.

teeth, good medical examinations, and good treatment of minor lesions. Good food—because most old people, inactive, often too idle, sitting and waiting, do not eat properly. The old man of Fig. 1 was taking only 1,200 calories a day before admission.

Good teeth—because in our experience most patients are edentulous and cannot masticate properly the foods they should have. The number presented at our clinic who are edentulous, without dentures, is far beyond average. Look beneath their tongues and you see the petechial hæmorrhages of multiple contusions where they have been masticating in parrot fashion. We believe the chronic irritation thus produced is the most important local factor in the production of malignancy. Perhaps second is diet, which is usually poor in protein and vitamin B.

Good medical examinations—because without the same type of meticulous, all-embracing routine in examining the mouth that we use for chest and abdomen we will miss the early lesions in curable stages.

Lastly, good treatment for early lesions—because thorough cauterization of all leukoplakias and hyperkeratoses cures future cancer. Excision biopsy of any doubtful tumour either is curative or leads to early radical treatment.

Reliable statistics show that 70-85% of oral cancer does not metastasize beyond the clavicle. In our 265 cases of the past two years we have seen only one in which metastases passed this bridge. Surely in this lies opportunity and challenge in combating these highly malignant cancers.

## SUMMARY

The treatment of cancer of the mouth is primarily surgical, with radiation reserved for very early intraoral and for lip lesions. The practice of routine combination of radiation and surgery to the primary lesion is condemned. Radical neck dissection is not indicated unless metastases are found in the neck. The assessment of the surgical risk is based on clinical experience alone. A feeding apparatus for use with a plastic tube in postoperative care is presented. A plea is made for thorough oral examination, oral prophylaxis and early biopsy of all doubtful lesions.

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# BRONCHOGENIC CARCINOMA—A FIVE-YEAR SURVEY*

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THE TUMOUR REGISTRY of the Montreal General Hospital was organized in 1950 for closer follow-up of pulmonary cancer. This survey covers the first five years. It is presented as a study of primary pulmonary carcinoma with particular emphasis on procedures and results. This study does not include bronchial adenoma, nor does it include "malignant adenoma".

A short review of the total series will give the general perspective. From the total number of cases a few of special interest will be extracted and commented upon. In the five years covered, 145 cases were registered with the tumour registry. Of these 127 were in men and 18 were in women, a ratio of 7 to 1. The average age was 62 years.

The following is a pathological classification, based on the final pathological observations—after autopsy, when available: epidermoid carcinoma 53, anaplastic carcinoma 37, adenocarcinoma 7, alveolar carcinoma 3, unclassified 15, unproven 30.

The unclassified cases are those not fitted into one group or another because of inadequate tissue specimens. Such specimens were obtained from sputum, bronchoscopic washings or bronchoscopic biopsy specimens too small or too badly crushed for further description, other than simply "carcinoma". The original number of "unclassifieds" was much larger, but was later clarified and reduced in number by subsequent re-examination of surgical specimens from post-mortem examinations.

The autopsy material was obtained from 58 cases. No autopsy was obtained in 79 cases, and 8 patients are still living.

A breakdown study of survival time is startling. Of 145 patients treated between January 1950 and December 1954, 137 are dead at the time of writing, and eight living. Of the 137 deaths, 45 occurred within a month of the time of diagnosis. Of these 45 early deaths, 36 were directly attributable to the carcinoma, the other nine to operative mortality and pulmonary embolism. Delayed diagnosis was not excessive. Of the 36 early deaths due to carcinoma, 32 took place within six weeks of the patient's appearance for diagnosis. This shows clearly that this series contains a group of patients who, for one reason or another, present themselves late for diagnosis.

The factors affecting survival time are hard to evaluate. Comparing treated and untreated cases is fallacious in part. A case is usually "untreated" because it is considered that no treatment will help the patient. At the other end only the most favourable cases are operated on. Radiotherapy is attempted only on those who will apparently live long enough to complete at least a palliative dose of radiation. In the broad sense, therapy (operation, irradiation, nitrogen mustard) is attempted only in those cases likely to live long enough to benefit. Hence by selection the survival figures are weighted in favour of therapy, and particular forms of therapy. For these reasons the figures on therapy and survival time will be given without further comment.

One hundred and forty-five cases presented. (Eight patients living will be considered separately.)

Fifty-six untreated (including unproven cases): average survival of less than two months after diagnosis.

Twenty-three given incomplete radiotherapy (i.e., inadequate for palliation, less than 3,000 r in four weeks): average survival of 2½ months.

Twenty-seven given complete radiotherapy (adequate for palliation, 3,200 r in four weeks minimum): average survival 8½ months.

Thirteen undergoing exploratory thoracotomy: Two with incomplete irradiation: 1 month and 4 months. Six with complete irradiation: two, 2 months; four, 6 months. Five without irradiation: one operative death and survivals of 2, 6, 9 and 18 months.

Sixteen undergoing pneumonectomy: One with incomplete irradiation: 4 months. Three with complete irradiation: 1 month, 1 year, and 3 years. Twelve without irradiation: four postoperative deaths and eight survivals (one for 1 month, two for 6 months, two for 1 year, two for 3 years, one for 4½ years).

Two chance autopsy findings.

As regards the eight survivors, details of management are as follows. Three are pathologically unproven. Five are pathologically proven and all are epidermoid carcinomas. Two treated by pneumonectomy alone are alive 12 months and four years later. Two treated by radiation alone are alive 15 months and 12 months later. One treated by preoperative radiation followed by operation is alive and well three years later.

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From the above 145 cases, seven are selected because of unusual features and features of general interest.

1. Mr. P.L., age 59. Admitted March 17, 1952, with hæmoptysis, loss of weight and strength. Films showed atelectasis of the left lower lobe. Bronchoscopy and biopsy on March 22 showed an epidermoid carcinoma of the left main bronchus, with extension to the carina, making it inoperable. Preoperative radiotherapy was given, starting on March 31 with 4,100 r T.D. in 47 days, through multiple 10 x 10 cm. fields. The atelectasis did not completely disappear.

A repeat bronchoscopy was negative on June 28, 1952. A pneumonectomy was carried out on July 15, 1952. Section showed only residual small islands of tumour in the posterior lower lobe branch bronchus. The patient has continued well since that time without evidence of recurrence.

2. Mr. H.G., age 58. Admitted March 11, 1951, with shortness of breath. Films showed a right hilar mass and atelectasis. Bronchoscopy showed the right main bronchus to be filled with tumour which extended to invade the carina and the trachea just above the carina. Biopsy section revealed an epidermoid carcinoma. Radiotherapy was given through 10 x 10 cm. fields to a T.D. of 5,500 r in 42 days. Subsequent bronchoscopic examinations and biopsies showed the carina and the right main bronchus to be clear. However, tumour was observed to be present below the area of treatment. This was a geographical miss in the sense that the tumour was larger than the area treated. The patient died February 1952. Autopsy was not obtained.

3. Mr. J.D., age 59. Admitted March 19, 1953, with chest pain and shortness of breath, radiography showing a left hilar mass. Bronchoscopy and biopsy on March 23 showed an epidermoid carcinoma, left main bronchus. He later developed a pleural effusion on the left. Radiotherapy was begun on April 8. A dose of 4,000 r in 37 days was given. The patient died on June 10 with a carcinomatous pericarditis. The autopsy specimen showed "no gross or microscopic evidence of residual primary tumour".

4. Mr. D.K., age 59. Admitted July 21, 1953 with a mass in the right hilar region but no positive biopsy. Bronchoscopy and sputum examinations were negative. Roentgentherapy through 8 x 10 cm. fields was given to a dose of 6,000 r in 62 days, beginning on August

Fig. 1.—P.L., age 59. Chest film, March 17, 1952. See case report.

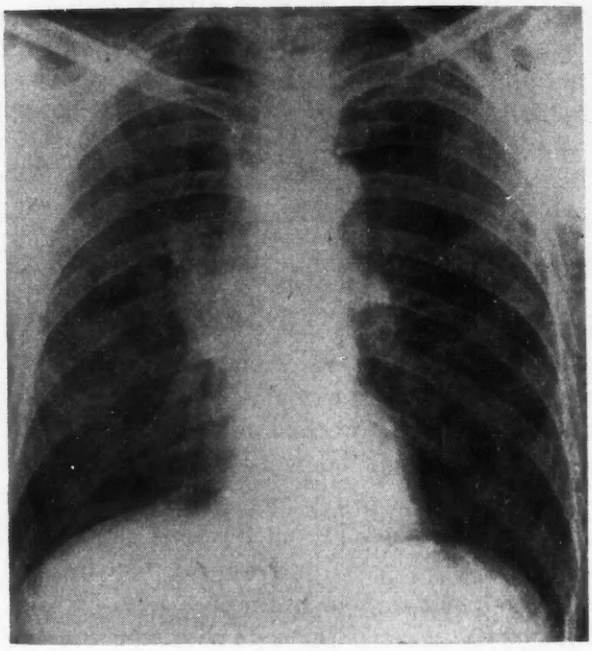

Fig. 2.—C.G., age 57. Chest film, March 15, 1954. See case report.

13. On April 3, 1954, a right pneumonectomy was carried out because of recurrent nodules in the periphery of the right lung. Residual tumour in the mediastinum not removed at operation was treated by roentgentherapy. Nodules were noted in the left lung before death. The patient died on July 14, 1954. An autopsy was not obtained but the operative specimen showed no tumour involving the walls of the bronchus. However, at the right hilus at the base of the stem bronchus to the right upper lobe, residual carcinoma was found in the lymph nodes adjacent to an area of puckered bronchial wall.

5. Mr. C.G., age 57. Admitted on March 15, 1954, with a history of epigastric pain and a chest film showing a right hilar lesion. Biopsy showed an anaplastic carcinoma. Thoracotomy was carried out on April 3 and found inoperable. Roentgentherapy was begun on April 6 and carried to a T.D. of 4,500 r in 39 days. Treatment was discontinued at this relatively low dose when a liver survey with radio-iodinated serum albumin (RISA) showed evidence of metastases in the region of the 12th thoracic vertebra. At the time of the RISA test, film examination of the spine was negative but a collapse of the vertebra subsequently developed. The metastases were treated by irradiation. Other areas of metastases developed, and the patient died on December 7, 1954. Autopsy showed residual hilar peribronchial and perivascular scarring without evidence of remaining tumour in the lung, peribronchial, hilar or mediastinal lymph nodes. The liver, pancreas, spleen, mesenteric and retroperitoneal lymph nodes were involved.

6. Mrs. J. V., age 59. Admitted on August 5, 1953, with extreme shortness of breath, and moved about by stretcher. Bronchoscopic biopsy showed an anaplastic carcinoma and treatment was begun on August 11. The patient was soon relieved of her dyspnœa and continued with the latter half of her treatment as an outpatient. A tumour dose of 5,300 r in 59 days was given, being completed on October 8, 1955. The patient died on October 16 of a massive fatal pulmonary embolus from utero-pelvic veins. The carcinoma observed at bronchoscopy had completely disappeared. The bronchial walls in the area of treatment were free of tumour. Tumour, apparently viable, was present outside the treated areas.

7. Mr. D.K., age 62. Admitted on June 30, 1954, with a history of chest pain, weight loss and cough, radiographs showing a left hilar lesion. Biopsy of a supra-

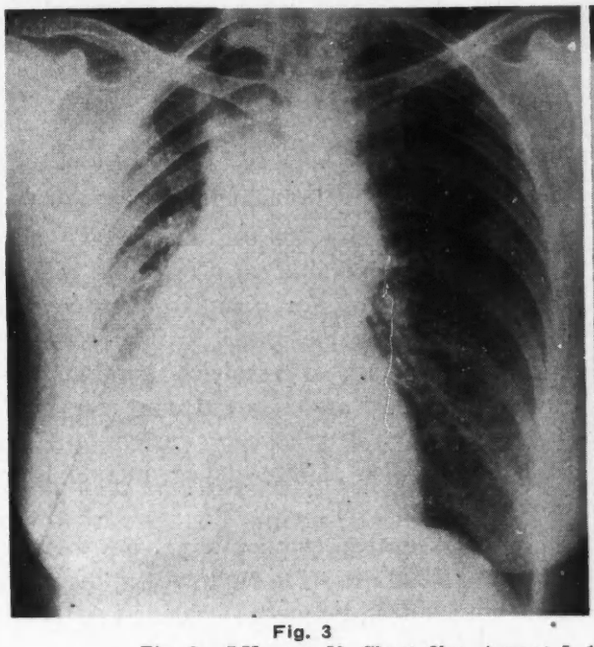

Fig. 3

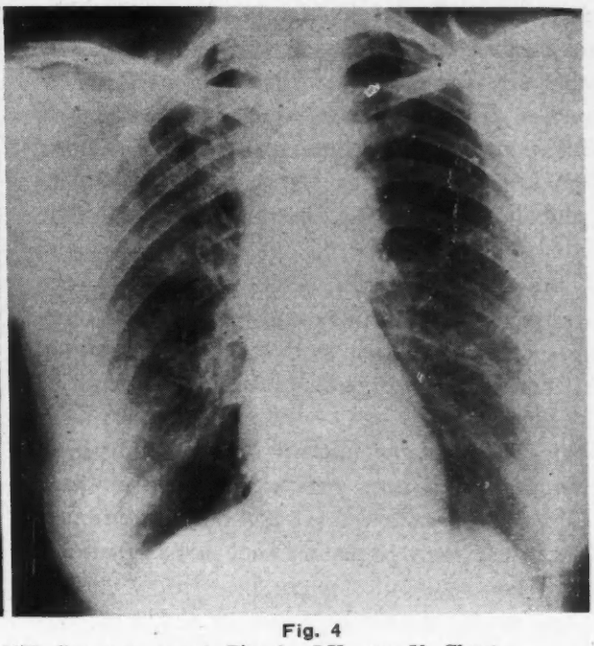

Fig. 4

Fig. 3.—J.V., age 59. Chest film, August 5, 1953. See case report. Fig. 4.—J.V., age 59. Chest film, October 8, 1953. Eight days before death. Note emboli in the right apex.

clavicular node showed an "undifferentiated carcinoma metastasis". Irradiation therapy was begun on July 26, a tumour dose of 6,100 r being given in 47 days, through multiple 10 x 10 cm. fields. The patient was freed of his pain and tolerated the treatment well but died of liver metastases. Autopsy showed radiation changes involving the lungs but no tumour. Metastases to the liver and upper abdominal lymph nodes were present.

### Special Comments

The comments on the surviving few have been made.

The alveolar cell carcinomas were typical in that an exact diagnosis was not made until post mortem.

The symptomatology was not evaluated statistically. Two items not usually listed in the literature are that a high proportion of these patients had a history of chronic cough, with or without a tobacco history. This cough antedated the disease so far that it could not have been a symptom of the disease.

Another startling feature is the frequency with which the patients complained only of general aches and pains and possibly an associated

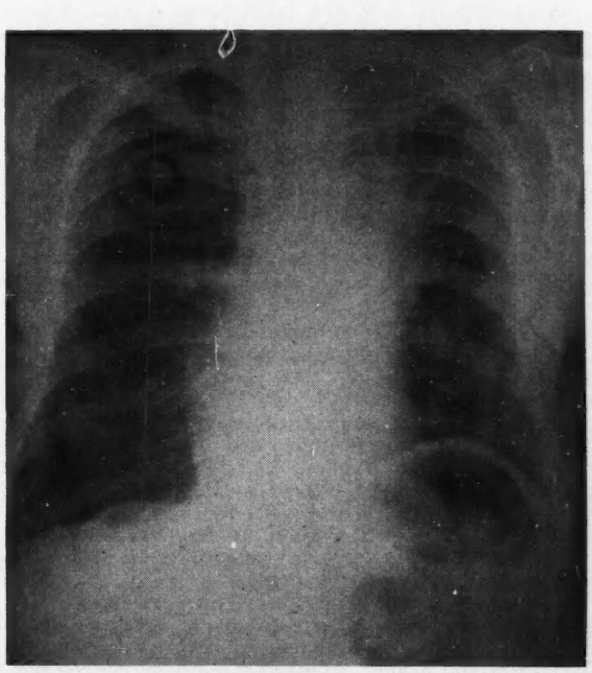

Fig. 5.—D.K., age 62. Chest film, June 30, 1954. See case report.

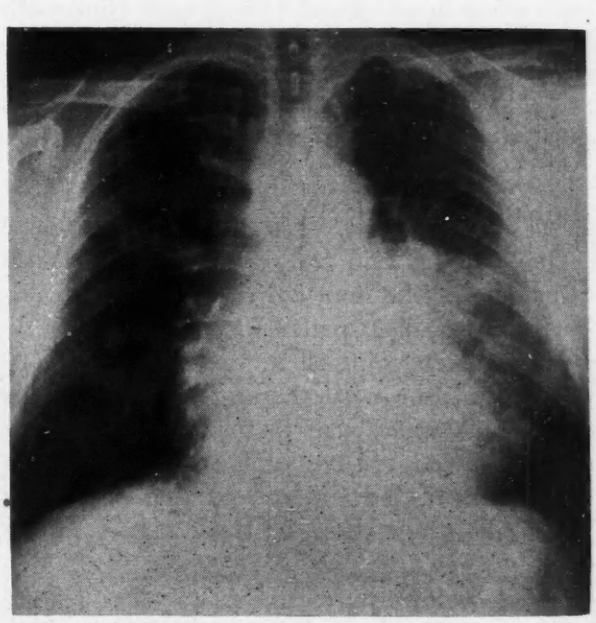

Fig. 6.—J.D., age 59. Chest film, March 19, 1953. See case report.

weight loss and occasional loss of appetite. The pains may be fleeting, occurring first in one side of the chest or the other, or in the back or extremities. There appears to be no correlation with the apparent anatomical sites of the disease. When bony metastases are present and radiographically obvious, the fleeting character of the pain is not present.

A surprising number were discovered accidentally, the patient presenting himself for complaints elsewhere such as dysphagia, abdominal pain, jaundice, joint pain, cardiac symptoms or even hæmorrhoids.

Many cases were initially labelled "atypical pneumonia" for some months before the diagnosis was finally proven. It has been mentioned before but it bears repeating that delayed resolution or recurrence of a pneumonia in patients of this age group should be taken as a sign of cancer.

Another point of interest is the bronchoscopic biopsy reports. Several times the initial biopsy reports were "squamous metaplasia". Additional search brought out the true malignant nature of the disease behind the fringe of "squamous metaplasia".

Twelve patients received a curative dose of radiation (4,500 r in six weeks minimum). Only seven came to autopsy or surgical resection. It is evident that the disease is adequately radiosensitive, but is too widespread at the time of initiation of treatment; all cancer-bearing areas cannot be treated. This observation has also been made in œsophageal carcinomas (Buschke).

It should be noted that our cobalt-60 teletherapy unit was not installed until May 1955, hence these cases received a conventional 250 kV radiotherapy with an h.v.l. of 2.5 mm. Cu.

## Summary

One hundred and forty-five cases of primary carcinoma of the lung are reviewed and evaluated statistically, pathologically, and therapeutically. The outlook in these cases is very poor, no matter what therapeutic procedure is used. Failures are due to the disease's having spread beyond the treatable area by the time treatment can be undertaken. Eight survivals are noted. Only three of these appear to be cures.

In all, radiotherapy appears to offer definite palliative value in suitable cases, and is an important adjunct to surgery in other selected cases.

## Conclusion

1. Roentgentherapy is of established value in the management of bronchogenic carcinoma.

2. Indications for its use are: (a) To make localized but inoperable cases operable (Cleland and Smithers). (b) For definitive treatment of technically inoperable cases. (c) For palliation, because atelectasis is resolved, superior vena cava syndromes are relieved and prevented, metastatic pain is relieved, effusions are controlled, and, also of importance, morale is improved.

3. The curative tumour dose lies between 4,500 and 6,000 r in six to eight weeks, the palliative tumour dose between 3,000 and 4,500 r in six weeks.

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## MEDICINE AND ADMINISTRATION

In an address delivered to a hospital management committee recently (*Lancet*, 2: 714, 1955) Sir Russell Brain had some interesting comments to make on the relationship between the physician and the administrator in medicine. He drew attention to the fact that the National Health Service required as much voluntary service in England as did the old voluntary hospital system, and that, although this was a good thing, there was a risk that the public-spirited voluntary workers were being overloaded. He deprecated the excessive criticism of hospital administrators and pleaded that these persons, often themselves doctors, should be given credit for at least as much understanding and commonsense as physicians claimed for themselves.

On the other hand, he pointed out that many people on hospital boards and management committees, coming for the first time into close contact with the work of doctors, do not understand the primary importance of preserving the independent professional status of the doctor, who undertakes duties and responsibilities completely unrelated to the source of his income. Although the doctor in England is paid by the State, and must therefore faithfully do the work for which he is paid, he has an absolute obligation to the patient, entirely beyond the scope of the employing authority, which has no right to dictate to the individual doctor on any matter of professional practice or ethics. This professional independence, said Sir Russell Brain, is not merely an exaggerated form of sectionalism; it is essential to the welfare of the health service and indirectly to the welfare of society.

# STEATORRHŒA FOLLOWING OPERATIONS ON THE GASTRO-INTESTINAL TRACT*

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DURING THE PAST five years we have found steatorrhœa in seven adults whose symptoms of this disorder appeared after operations on the gastrointestinal tract. These patients presented one or more of the following conditions: weight loss, unexplained megaloblastic anæmia, iron deficiency and osteomalacia. Steatorrhœa was demonstrated in each case by fat-balance studies.

symptoms had appeared after an operation on the gastrointestinal tract. Partial gastrectomy had been performed on five. One had a jejuno-colic fistula. The remaining patient was left with a colonic cul-de-sac after resection of the lower ileum and anastomosis to the transverse colon. Surgery preceded the onset of symptoms by one to 14 years.

The salient clinical and laboratory findings are shown in Table II.

## CASE REPORTS

CASE 1.—A 36-year-old woman had had a partial gastric resection 14 years previously. Peptic ulcer had been suspected but no lesion was found. She presented with weight loss and megaloblastic anæmia (red cell count 3.6 million; hæmoglobin value 12.5 g. per 100 ml.). A sternal puncture showed megaloblastic bone marrow. She had diarrhœa with five to 10 pale mushy stools daily. Her tongue was smooth and red. There was no free HCl in the gastric juice. There was no neurological disorder.

TABLE I.

BOWEL ABNORMALITIES AND PRESENTING CONDITIONS

| *Case* | *Sex and age* | *Presenting conditions* | *Duration of symptoms* | *Type of operation* |
|---|---|---|---|---|
| 1 | F. 36 | Megaloblastic anæmia, weight loss | 4 years | Partial gastrectomy 14 years. |
| 2 | M. 59 | Megaloblastic anæmia, weight loss | 6 years | Jejuno-colic fistula 11 years. |
| 3 | M. 27 | Megaloblastic anæmia, weight loss | 5 years | Ileal resection and colonic "cul-de-sac" 6 years. |
| 4 | M. 52 | Megaloblastic anæmia, osteomalacia | 1 year | Partial gastrectomy 8 years. |
| 5 | M. 56 | Iron-deficiency anæmia, weight loss | 1 year | Partial gastrectomy 10 years. |
| 6 | M. 29 | Iron-deficiency anæmia | 1 year | Partial gastrectomy 6 years. |
| 7 | M. 60 | Iron-deficiency anæmia, weight loss | 1 year | Partial gastrectomy 15 years. |

*Description of cases.*—The bowel abnormalities, presenting symptoms and their duration, together with the sex and age of each patient, are shown in Table I. There were six men and one woman. Their ages ranged from 27 to 60 years. Three had megaloblastic anæmia and weight loss, two iron-deficiency anæmia and weight loss, one megaloblastic anæmia and osteomalacia and one iron deficiency alone. Symptoms had been present for one to six years before the patient came under our observation. Three of the patients gave a history of diarrhœa with pale, bulky, frothy, offensive stools. In the other four, this distinctive sign was absent. None of the patients had lived in the tropics. A clear history of cœliac disease in childhood was not obtained from any of them. In each case the

CASE 2.—A 59-year-old man had had two feet (60 cm.) of the lower ileum resected and an anastomosis established between the jejunum and colon 11 years previously. These operations were undertaken after traumatic rupture of the sigmoid colon. He presented with severe megaloblastic anæmia and marked weight loss. The red cell count was 1.8 million and the hæmoglobin level 8.6 g. A sternal puncture showed megaloblastic bone marrow. He had diarrhœa with four to six soft pale stools daily. Free HCl was present in the gastric juice. The prothrombin time (24 seconds, Quick) was elevated. There was no glossitis and no neurological disorder.

CASE 3.—A 27-year-old man had been crushed under a truck six years previously. This necessitated resection of the lower two-thirds of the small bowel, the entire cæcum and half the ascending colon. An anastomosis was fashioned between the remaining small bowel and the transverse colon, producing a colonic cul-de-sac. He presented with marked weight loss and severe megaloblastic anæmia (red cell count 1.2 million; hæmoglobin 4.5 g.). A sternal puncture showed megaloblastic bone marrow. He had a smooth red tongue. There was clubbing of the fingers and toes. Free HCl was present in the gastric juice. He was passing 10 to 12 pale, bulky, frothy, foul-smelling stools daily. There was no neurological abnormality.

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CASE 4.—A 52-year-old man had had a partial gastric resection for duodenal ulcer eight years previously. He presented with severe bone pain and megaloblastic anæmia (red cell count 2.8 million; hæmoglobin 9.7 g.). A sternal puncture showed megaloblastic bone marrow. There was no free HCl in the gastric juice. There was no glossitis and no neurological disorder. He did not have diarrhœa. He had second-degree osteomalacia.[1] The serum calcium level (6.0 mg. per 100 ml.) was low. The serum inorganic phosphorus level (2.6 mg. per 100 ml.) was normal. The serum alkaline phosphatase level (11.4 Shinowara units per 100 ml.) was elevated. X-ray examination did not show decalcification of the bones. There was no evidence of renal disease.

TABLE II.

CLINICAL AND LABORATORY FINDINGS

| Case | Weight loss | Anæmia: Megaloblastic | Anæmia: Iron deficiency | Osteomalacia | Glossitis | Prothrombin deficiency | Free gastric HCl | Clubbing |
|---|---|---|---|---|---|---|---|---|
| 1 | + | + | 0 | 0 | + | 0 | 0 | 0 |
| 2 | + | + | 0 | 0 | 0 | + | + | 0 |
| 3 | + | + | 0 | 0 | + | 0 | + | + |
| 4 | + | + | 0 | + | 0 | 0 | 0 | 0 |
| 5 | + | 0 | + | 0 | + | 0 | 0 | 0 |
| 6 | + | 0 | + | 0 | + | 0 | 0 | 0 |
| 7 | + | 0 | + | 0 | 0 | 0 | + | 0 |

CASE 5.—A 56-year-old man had had a partial gastrectomy for duodenal ulcer 10 years previously. He presented with weight loss and iron-deficiency anæmia (red cell count 3.0 million; hæmoglobin 7.8 g.). The serum iron (25 $\gamma$ per 100 ml.) was low and the unsaturated iron binding capacity (500 $\gamma$ per 100 ml.) was high. Sternal puncture showed normoblastic bone marrow. He had glossitis. There was no history of blood loss and no evidence of occult bleeding. There was no free HCl in the gastric juice. He did not have diarrhœa.

CASE 6.—A 29-year-old man had had a partial gastrectomy six years previously because of hæmorrhage from a duodenal ulcer. There was no history of subsequent blood loss. He presented with iron-deficiency anæmia (red cell count 3.8 million; hæmoglobin 8.7 g.). The serum iron (13 $\gamma$) was low and the unsaturated iron binding capacity (450 $\gamma$) was high. A sternal puncture showed normoblastic bone marrow. He had glossitis. There was no evidence of occult bleeding. There was no free HCl in the gastric juice. He did not have diarrhœa.

CASE 7.—A 60-year-old man had had a partial gastric resection for duodenal ulcer 15 years previously. He presented with weight loss and iron-deficiency anæmia (red cell count 2.7 million; hæmoglobin 7.2 g.). The serum iron (10 $\gamma$) was low and the unsaturated iron binding capacity (400 $\gamma$) was high. A sternal puncture showed normoblastic bone marrow. There was no history of blood loss and no evidence of occult bleeding. Free HCl was present in the gastric juice. He did not have diarrhœa.

### FAT-BALANCE STUDIES

Observations were made over a 12-day balance period in five cases and over six-day and eight-day periods in the other two. In the three cases with diarrhœa this symptom had been controlled before the balance study was undertaken. The daily diet contained 75 g. of fat, 60 g. of protein and 360 g. of carbohydrate as calculated from food tables;[2] 70 g. of the fat was contributed by three foods—milk, butter and eggs. The patients received this diet for three days before the balance studies and throughout the studies. Carmine was used to mark the collection periods. The entire balance collection was mixed with water to a uniform creamy consistency. Duplicate 150-ml. aliquots were dried to constant weight.* Fat was estimated gravimetrically after Soxhlet extraction with ethyl ether. Nitrogen was estimated by the Kjeldahl method.

The results are shown in Table III. Daily fæcal fat ranged from 8 to 53 g., representing 11 to 71% of the intake. These data clearly indicate the presence of steatorrhœa in every case. In normal adults on daily intakes of 50 to 200 g. of fat, the fæcal loss is always less than 10% of the intake.[3-6]

In six cases the daily fæcal nitrogen output ranged from 0.8 to 1.6 g. These values are normal[4-6] and exclude pancreatic origin of the steatorrhœa. In the remaining patient (Case 3) the daily fæcal nitrogen was increased. Pancreatic dysfunction resulting from the injury cannot be excluded in this case.

*Treatment.* — Substantial improvement was achieved in all the cases by measures commonly used in the treatment of idiopathic steatorrhœa. Megaloblastic anæmia was corrected by parenteral concentrated liver extract in one case, parenteral vitamin $B_{12}$ in two cases, and a combination of oral folic acid and parenteral vitamin $B_{12}$ in one case. Iron-deficiency anæmia responded well to iron by mouth. Calcium lactate

*In some instances an extra aliquot was acidified before drying. This did not affect the nitrogen values.

and vitamin D by mouth corrected the osteomalacia in the one case in which this complication occurred. Diarrhœa was controlled by moderate restriction of dietary fat and large doses of calcium lactate by mouth. All the patients gained some weight, but preoperative levels were never attained.

TABLE III.

FAT BALANCE STUDIES

| Case | Balance period days | Stools per day | Fæcal fat g./day | Fæcal fat % intake | Fæcal nitrogen g./day |
|---|---|---|---|---|---|
| 1 | 12 | 1 | 12 | 16 | 1.5 |
| 2 | 12 | 1 | 13 | 17 | 0.8 |
| 3 | 6 | 1 | 53 | 71 | 4.0 |
| 4 | 12 | 1 | 17 | 23 | 1.6 |
| 5 | 12 | 1–2 | 12 | 16 | 1.3 |
| 6 | 8 | 1–2 | 12 | 17 | 1.9 |
| 7 | 12 | 1–2 | 8 | 11 | 1.2 |

In addition to these measures, corrective surgery was attempted in two cases. In Case 2, the jejuno-colic anastomosis was taken down and continuity of the bowel was thus restored. Medical therapy was discontinued at that time. Four years later fæcal fat excretion remains high and he is still underweight but the megaloblastic anæmia has not recurred. In Case 3, the colonic cul-de-sac was excised. Sufficient time has not yet elapsed to evaluate the results.

## DISCUSSION

The manifestations of the steatorrhœa which follows operations on the gastrointestinal tract are protean. In our cases they included weight loss, megaloblastic anæmia, iron deficiency, bone pain, glossitis, hypocalcæmia, osteomalacia, prothrombin deficiency, and clubbing of the fingers and toes. Diarrhœa is not always present. In four of our cases the steatorrhœa was latent.[7] Identical manifestations are encountered in idiopathic steatorrhœa.

The mechanisms by which operations on the gastrointestinal tract produce this syndrome are obscure. It used to be thought that removing or by-passing part of the gut simply decreased the total absorbing area and thus caused steatorrhœa. It is now known that removal of several feet of small bowel does not produce steatorrhœa, provided an end-to-end anastomosis is performed.[8] In a gastro-colic or entero-colic anastomosis, only a small proportion of ingested material passes directly through the fistula; most of it travels through the by-passed loop.[9] Stagnation of bowel contents with changing bacterial flora may be an important factor.[10, 11] Stagnation does occur in a by-passed loop, in a cul-de-sac or above a partial stricture. One of our cases had a by-passed loop resulting from the jejuno-colic anastomosis. One had a colonic cul-de-sac. Each of the other five had a partial gastric resection with anastomosis of the remaining stomach to the jejunum leaving a duodenal cul-de-sac.

Cases of steatorrhœa after operations on the gastrointestinal tract are being reported with increasing frequency. It seems likely that this is by no means a rare disorder. Elucidation of the mechanisms concerned in its production might shed light on the pathogenesis of steatorrhœa and the sprue syndrome in general.

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## FORTHCOMING C.M.A. MEETINGS

1956 Quebec—June 11-15 (Ecole de Commerce).
1957 Regina—June 17-21.
1958 Halifax—June 15-19.
1959 Edinburgh—July 16-24.
(Conjoint Meeting with B.M.A.)
1960 Banff—June 13-17.

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# LARYNGOCŒLE*

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A LARYNGOCŒLE is an anomalous air sac which develops from the saccule of the laryngeal ventricle. An extensive review of the literature on this subject has already appeared in a number of recent excellent articles.[1, 2] With a few exceptions, only those authors whose contributions have a direct bearing on the phase of the subject under discussion will be mentioned.

Larrey[3] described this anomaly in 1829 and is usually credited with being the first surgeon to call attention to it. Although the number of cases reported is still not large, in recent years laryngocœle has been more frequently mentioned, probably because of more accurate diagnosis.

Large air sacs communicating with the laryngeal ventricle are normally present in certain animals, such as the chimpanzee, orang-outang and the gorilla (Fig. 1). In these animals, according to Negus,[4] these air sacs serve a useful purpose in that they act as reservoirs which can be used for mixing and rebreathing of air. Most of these sacs in the lower animals lie under a layer of muscle which, in its contraction for other purposes of bodily activity, expels the retained air and forces it back into the lungs in a mixed condition, to be used further in respiration. Again quoting Negus:

> The opening is beneath the downturned ventricular band, or superior thyro-arytenoid fold. These sacs are employed at times of great bodily activity or anger, when the animal wishes to use its forelegs for defense or aggression. Having filled its lungs, the animal is able to direct the air at the next expiration into the laryngeal sacs, if it closes its mouth and nose or its ventricular bands. Here is seen, if this explanation is correct, a mechanism of mixing and automatic rebreathing, with conservation of energy and without the diversion of muscles for respiration, when they are required for other purposes.

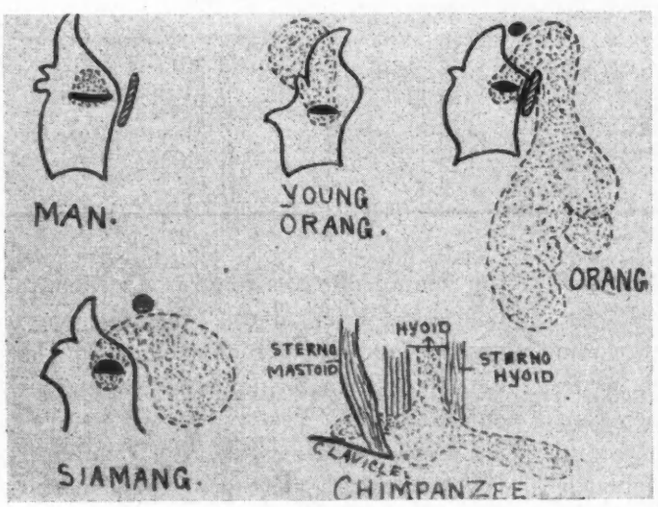


Fig. 1

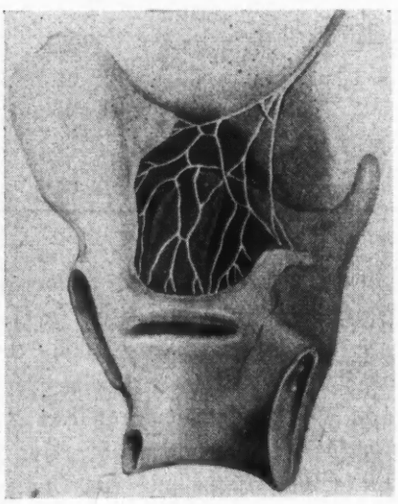

Fig. 2

Fig. 1.—Ventricles and ventricular air sacs (after Negus). Fig. 2.—Section through the thyroid and cricoid cartilages showing the right sacculus (after Hilton).

It is doubtful if these sacs act as an accessory vocal organ, as many animals with large sacs are relatively silent, whereas others with small sacs are very noisy. In man, these sacs are not normally present but many of the species are far from silent.

In man, the saccule of the laryngeal ventricle extends upward from the anterior part of the ventricle. It is apparently always present, but varies greatly in size and shape. As described by Moore,[5] "sometimes it is nearly conical with its base below, in other cases it is pear-shaped, with its broader part above; occasionally, it is nearly cylindrical" (Fig. 2). It only occasionally rises higher than the upper border of the ala of the thyroid cartilage. It seems probable that the saccule, which is a constant finding in man, is a degenerated relic of the large air sacs present in some other animals. Variations in the size of the saccule might account for asymmetry of the ventricular bands, which is not an uncommon clinical finding. The saccule contains

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numerous mucus glands and no doubt supplies much of the mucus necessary to keep the edges of the vocal cords moist during phonation.

The thyroepiglottic and aryepiglottic muscles as they sweep into the aryepiglottic fold surround the upper part of the saccule. Moore[5] in one of his illustrations draws attention to the fact that, below the lower fibres of the aryepiglottic muscle, there is a weak triangular space. It is possible that a hernia of the saccule might protrude through this area (Fig. 3).

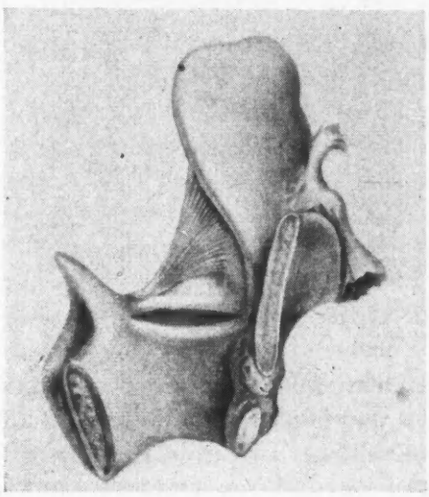

Fig. 3.—Section through the right side of the thyroid and cricoid cartilages. Note the weak triangular area below the lower fibres of the aryteno-epiglottideus muscle (after Hilton).

The presence of a congenitally long saccule is probably the most important factor in the development of this anomaly. This would seem a reasonable supposition if the saccule extends beyond the limits of the thyroarytenoid muscles. As mentioned previously, it is possible that an internal laryngocœle may protrude into the triangular space below the aryepiglottic muscle.

Although pre-existing pathological lesions do not appear to play a part in most cases, they probably do in some. It is possible that tumours, cysts and inflammatory lesions may produce a check-valve mechanism at the orifice of the ventricle, allowing the sac to be inflated, but interfering with deflation. This is suggested but not proven by the fact that a laryngocœle is sometimes associated with cancer of the larynx. A case of this type was reported by Schall[8] in 1944. If routine x-ray studies of pathological laryngeal conditions were made, this condition might be found more frequently.

Increased intralaryngeal pressure still appears, however, to be a factor common to many reported cases. The ventricles are obviously subjected to increased pressure during sneezing, nose blowing, blowing wind instruments, etc. That this also obtains during other activities is shown by Lindsay.[7] He demonstrated by roentgenological examination, using the planigraph, the position and shape of both the true and false cords during the performance of certain functions of the glottis. These studies demonstrated that during strenuous muscular activity with the upper extremities the glottis is firmly closed by both false and true cords, and the tracheal lumen is increased in size, indicating increased intratracheal pressure. During still more strenuous closure of the glottis, as in straining at stool or during severe coughing bouts, both false and true cords are shown to be in apposition. In some views, however, the ventricle is plainly seen and in some there appears to be more firm apposition of the ventricular bands than of the true cords.

These studies show that during certain activities the glottis is firmly closed and the intratracheal pressure increased. They also suggest that this increase in pressure is transmitted to the ventricles, as the true cords offer less resistance than the upper sphincter of the larynx.

Considering the numerous conditions that cause increased intratracheal pressure and the relatively infrequent occurrence of laryngocœle, it would appear that the presence of a congenitally long saccule is the most likely primary etiological factor.

In 1900, Pelletier[6] divided these air-sacs into two groups or types: (1) intralaryngeal and (2) a group of cases in which one portion of the tumour is intralaryngeal and the other extralaryngeal. More recently, Lindsay[7] has divided them into three groups: (1) the internal laryngocœle, in which the cystic dilatation appears within the larynx; (2) the superior external laryngocœle, in which the sac has perforated the thyrohyoid membrane and appears as a swelling in the neck; (3) a combined internal and external laryngocœle. Some authors doubt that there is a true "external" type, maintaining that the "external" type is always combined with an "internal" laryngocœle and is therefore a "combined" one.

The clinical features of the laryngocœle vary greatly, depending on the location and size and also on the presence or absence of infection in the sac. They can be summarized as follows:

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1. Voice changes. Hoarseness is a common symptom in internal laryngocœle, but variations in the size of the lesion may cause this to be intermittent.
2. Cough is also frequently present.
3. Shortness of breath. This also depends on the size of the internal laryngocœle and will probably be variable.
4. Swelling in the neck. This presents above the thyroid ala and may extend as far laterally as the sternomastoid muscle. The size of both internal and external laryngocœles is usually increased by the Valsalva manœuvre and by swallowing, coughing and straining. They frequently deflate on quiet respiration and can usually be deflated by gentle pressure. Deflation may be accompanied by an audible escape of air into the larynx. Pathological lesions in the larynx may cause a check-valve mechanism and make deflation difficult or impossible.
5. Pain and local tenderness will be present if the sac becomes very large or becomes infected.
6. Mild headache may occur due to venous obstruction.

## DIAGNOSIS

Diagnosis is made by observing any or all of the above features. Mirror laryngoscopy may reveal very little if the internal laryngocœle is deflated. When inflated, it presents as a smooth cystic swelling in the region of the ventricular band. This swelling may extend into the aryepiglottic fold and even up to the base of the tongue, or into the piriform sinus. Corroborative evidence, such as the demonstration of air cysts in the larynx or neck by roentgenological examination, is of great help and may eliminate the need for diagnostic aspiration or the instillation of radio-opaque media.

## PATHOLOGY

Laryngocœles are usually unilateral but may be bilateral. They have been demonstrated in the young, but most reported cases are in male adults. Most authors appear to agree on the location and extension of internal laryngocœles.

External laryngocœles, according to most reports, herniate through the thyrohyoid membrane and extend laterally superficial to this membrane and deep to the infrahyoid muscles (Fig. 4). On the other hand Harrison[9] says:

> Many accounts state that the laryngocœle actually herniates through the membrane, but from personal observation the sac passes upward deep to the membrane, as there is no obstruction to its progress. The swelling eventually passes into the more superficial structures of the neck deep to the lateral border of the thyrohyoid membrane. In this region, there is a dehiscence between the edges of the middle and inferior constrictor muscles and I consider this is the point through which the laryngocœle passes.

This difference of opinion may be simply a different interpretation of observations. On the other hand, it is quite possible that some laryngocœles may follow the course suggested by Harrison, and others herniate through the thyrohyoid membrane. In the bilateral case which I am reporting the sac certainly appeared to herniate through the membrane.

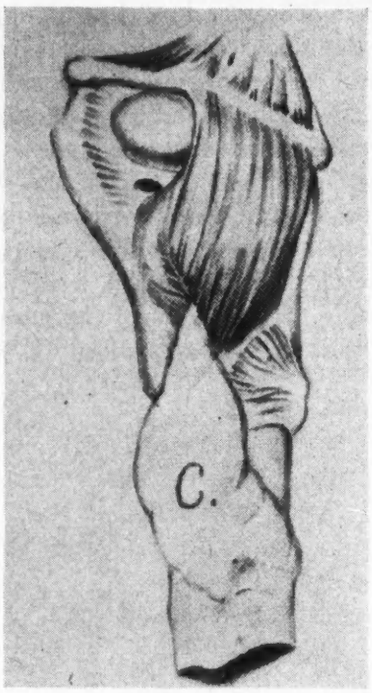



Fig. 4.—A right extralaryngeal ventricular sac (after Freedman).

The complication of infection in laryngocœles is always liable to occur. It usually occurs during throat infections and, when present, is always a source of danger.

## TREATMENT

Few surgeons, if any, have managed a sufficient number of cases to justify their drawing definite conclusions as to the best method of treatment. There is even a difference of opinion on which cases should be treated. It has been stated that "only laryngocœles causing distress to the patient require operation". It is questionable whether this is a wise dictum, as an internal laryngocœle may at any time enlarge sufficiently to interfere with the laryngeal airway. This is especially liable to occur if the sac becomes infected. This complication (i.e., infection) has, I think, been reported frequently enough to warrant surgical intervention even in cases without distressing symptoms. The operation is also a more simple and safe procedure if done before infection intervenes.

Although there is considerable variance of opinion on details of treatment, it is generally

agreed that the best surgical approach is an external one. Endolaryngeal treatment, such as puncturing the sac or cauterization through the laryngoscope, has been frequently attempted but has not proven satisfactory.

In the treatment of internal laryngocœles, some surgeons prefer an intralaryngeal operation through a laryngofissure. The majority, however, advocate an extralaryngeal dissection after splitting the thyroid ala or removing part of it.

External laryngocœles are best approached through a transverse incision parallel to and below the ramus of the mandible. The sac, unless deflated, is usually easily found either under the infrahyoid muscles or lateral to them. It is most easily dissected from the fundus toward the midline. Many reports state that the sac is followed to the point at which it disappears under the thyroid ala where it is then excised. This entails leaving the saccule. Would it not be better to remove also the saccule in these cases, as one would in the treatment of the combined type?

In the treatment of combined external and internal laryngocœles, a few authors advise a two-stage operation. It can, however, be quite satisfactorily performed in one stage. The external part is dissected out first. The internal part is then followed down to the ventricle. Some surgeons claim that this can be done without splitting the thyroid ala, but dissection is facilitated by either splitting the ala or removing a notch or window from its anterior superior border.

Local anæsthesia has certain advantages if the patient will tolerate it. Not infrequently when the patient relaxes under general anæsthesia the sac deflates and may be difficult to find. Under local anæsthesia the patient can usually cooperate by reinflating it, if necessary.

## CASE REPORT

*Bilateral combined internal and external laryngocœle.*—Freedman,[10] a member of our staff, previously reported two cases from other hospitals. The following case is, as far as I know, the first one treated by the Department of Otolaryngology of our hospital.

G.H., a 23-year-old male, was admitted to the Montreal General Hospital in September 1953. His complaints were of a recurring soft tumour in the right side of the neck (Fig. 5) and shortness of breath. The latter coincided with the swelling of his neck.

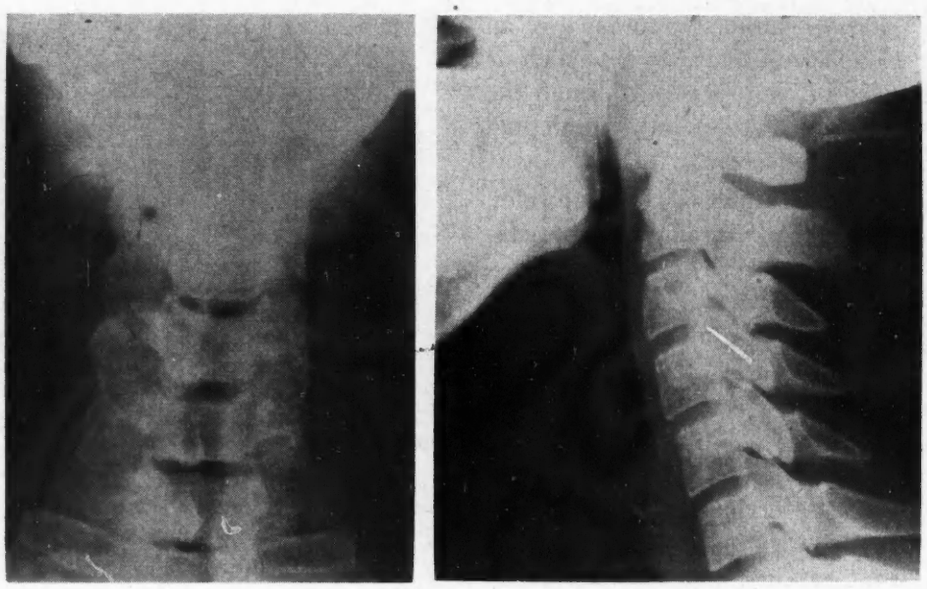
Fig. 5.—Photograph of patient showing the laryngocœle on the right.

This patient had laryngeal obstruction at birth and required an emergency tracheotomy. Attempts to dilate his larynx were unsuccessful and he wore a tracheotomy tube for three years. In 1942, at the age of 12, he again developed laryngeal obstruction, and a round swelling was noted on the left side of the larynx. After tracheotomy a biopsy was attempted. Thick mucoid material was seen to issue from the biopsy site and a diagnosis of cyst of the left ventricle was made. This procedure gave temporary improvement, but dyspnœa recurred about one year later. A laryngofissure was performed and a large cyst removed from the left side of the larynx. After this procedure, fixation of the left vocal cord was noted.

In 1950 he first noticed a tender lump on the right side of his neck. This became larger when he talked or swallowed, and could be deflated with gentle pressure. He did not complain of any laryngeal obstruction until September 1953, when he noted dyspnœa in association with the swelling. At this time the swelling on the right side of the neck was much larger.

Laryngeal examination showed a smooth swelling in the region of the right false cord and aryepiglottic fold. The left vocal cord was fixed, and the false cord region on this side was also a little full. The swelling of the right side of the larynx plus the fixation of the left cord resulted in a very small laryngeal airway.

X-ray examination of the neck showed a bilateral laryngocœle (Figs. 6a and 6b), the one on the right being quite large. On October 1, 1953, a tracheotomy was performed and the right laryngocœle was removed under local anæsthesia. A transverse incision was made parallel to and below the mandible. This extended from the sternomastoid muscle to the midline. A short longitudinal incision was also made just to the right of the midline over the right thyroid ala. This incision joined the medial end of the first incision. The infrahyoid muscles were divided and the laryngocœle came into view. It extended laterally to the sternomastoid muscle. The sac was freed by starting at the sternomastoid muscle and working toward the midline. It passed superficial to the superior horn of the thyroid ala and was easily separated from the thyrohyoid membrane. It then disappeared under the thyroid ala near the midline. At this point a small window of cartilage was removed (Fig. 7), and the sac was followed down to the right laryngeal ventricle. The removal of this piece of cartilage facilitated the dissection of the internal part. By this time the sac was deflated and the internal part was found to be quite narrow. It was ligated and severed close to the ventricle. When the window of cartilage was removed, the underlying inner perichondrium was saved and was sewn over the pedicle as a reinforcement. The sac, when reinflated after removal (Fig. 8), measured approximately 5 x 3 cm.



A B

Fig. 6.—Roentgenograms of bilateral laryngocœle. (A) Antero-posterior view. (B) Lateral view.

Fig. 7.—Lateral view of larynx—showing area (A) from which piece of cartilage is removed.

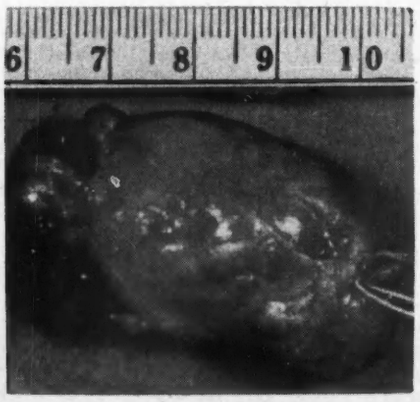



Fig. 8.—Right laryngocœle (reinflated).

The patient made an uneventful recovery, but while still convalescing from the operation he noticed that the swelling on the left side was increasing. His tracheotomy tube had been removed, but it was necessary to replace it as dyspnœa recurred about three or four weeks after the first operation. Laryngeal examination showed that the swelling of the right side of the larynx was gone but he now had definite swelling on the left.

On December 1, 1953, the left laryngocœle was removed by an operation essentially similar to that previously performed on the right side. The laryngocœle on this side was found to be slightly smaller than the one on the right. Recovery was uneventful except for pain referred to both ears, presumably caused by irritation of the superior laryngeal branch of the vagus. This postoperative pain was of short duration on the left side but persisted on the right. It was eventually relieved by an alcohol injection of the right superior laryngeal nerve.

## SUMMARY

A case of a bilateral combined internal and external laryngocœle is reported.

A brief résumé of different methods of treatment is given.

These lesions can apparently be treated satisfactorily by a one-stage external operation without opening the larynx.

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# THE INCREASE IN SERIOUS STAPHYLOCOCCAL INFECTIONS AS SHOWN BY POST-MORTEM INVESTIGATION*

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IN RECENT YEARS staphylococcal infections have become a serious problem in a hospital community. The high carrier rate and the resistance of the causative organism, *Micrococcus pyogenes* (Staphylococcus), to antibiotics have largely been blamed for the situation. As a result, greatest attention has been directed toward the appearance of antibiotic-resistant staphylococci, and this has been dealt with in a number of reviews, particularly those of Prissick[1] and of Welch.[2] Jackson[3] and his associates were among the first to point out the potentialities of the staphylococcus as a dangerous pathogen when they reported that of 91 cases of pneumococcal pneumonia, 7 died of staphylococcal infection following treatment with oxytetracycline. It is the purpose of this report to emphasize that this organism can become markedly virulent in individuals who have a lowered resistance due to some underlying condition which renders them susceptible to secondary infection.

It is routine procedure in this hospital to culture specimens of heart's blood and swabs taken from the cut surfaces of lungs and other infected areas of all cases coming to autopsy. The results of 213 cases are shown in Table I, and the sites of origin of *Micrococcus pyogenes* in Table II.

These results are most striking in view of the fact that the records of 1950 (311 autopsies) show three cases of bronchopneumonia and two cases of septicæmia due to staphylococci, although this figure may be low since it was not routine practice at that time to take specimens from all autopsies. With the exception of three patients who were admitted with a diagnosis of staphylococcal septicæmia, all the infections are considered to be secondary to other obvious debilitating features. The staphylococcal infection was not the primary cause of death but the terminal event in the course of some major disease.

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TABLE I.

AUTOPSY CULTURES

| *Organism isolated* | *No. of cases* |
|---|---|
| *Micrococcus pyogenes* | 87 |
| *Diplococcus pneumoniæ* | 4 |
| *Klebsiella pneumoniæ* | 3 |
| *Streptococcus pyogenes* | 1 |

TABLE II.

SITE OF ORIGIN OF *Micrococcus pyogenes* AT AUTOPSY

| *Specimen taken from* | *No. of cases* |
|---|---|
| Heart's blood | 2 |
| Lungs | 64 |
| Heart's blood and lungs | 14 |
| Kidneys | 3 |
| Meninges | 1 |
| Pericardial sac | 1 |
| Subdiaphragmatic abscess | 1 |
| Appendix | 1 |

Bacteriophage typing was used in an attempt to determine a possible relationship among the organisms isolated. If infection from carriers or other sources within the hospital had occurred, a predominant phage type would appear. The phage-groups of 52 of the strains are recorded in Table III.

TABLE III.

PHAGE GROUPS

| *Phage group* | *Per cent* |
|---|---|
| I | 23 |
| II | 4 |
| III | 61 |
| IV | 6 |
| Untypable | 6 |

The greatest percentage of strains belonged to Group III. Since this is a broad group, it is significant that 50% of the Group III staphylococci belonged to a single phage type—47.

The staphylococci isolated were tested for sensitivity to penicillin, oxytetracycline, chlortetracycline and chloramphenicol. The following results were obtained:

| | |
|---|---|
| Sensitive to all antibiotics | 18% |
| Sensitive to all antibiotics except penicillin | 30% |
| Sensitive to chloramphenicol only | 52% |

This represents a high percentage (82%) of penicillin-resistant staphylococci. The most important group, however, is the one which is

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sensitive to chloramphenicol but resistant to oxytetracycline, chlortetracycline and penicillin. This is the antibiotic pattern most commonly reported in this hospital. It is interesting that no strains were encountered which were resistant to all the antibiotics tested, and this is fortunately also true of strains identified from the hospitalized patient. Whether this situation will continue with the increased use of chloramphenicol is doubtful.

### CONCLUSIONS

1. *Micrococcus pyogenes* (Staphylococcus) has replaced *Diplococcus pneumoniæ* and *Streptococcus pyogenes* as the cause of terminal bronchopneumonia.

2. In a hospital community there is increased opportunity for staphylococcal infections from a variety of sources. The predominant strain isolated in this investigation was one sensitive to chloramphenicol and resistant to other antibiotics.

3. The potentialities of the staphylococcus as a virulent pathogen should not be overlooked, and treatment of infections with a specific antibiotic should be vigorous.

The authors wish to thank Miss L. Martin of the Quebec Ministry of Health, Division of Laboratories, for the phage typing of the staphylococci.

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# REACTIONS TO LOCAL ANÆSTHETICS*

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TOXIC REACTIONS to local anæsthetics are fortunately rare, but whatever the route of administration or the drug used, the possibility of their occurrence must not be ignored. The widespread use of cocaine following its introduction to medicine by Köller in 1884 led to numerous reports of its toxicity. In 1890, Falk[1] collected 176 cases of acute intoxication of which 10 were fatal. Procaine, a much less toxic drug, was introduced in 1905 by Einhorn, and its continued popularity throughout over half a century is testimony to its safety. Countless attempts have been made to synthesize drugs which, while still retaining the low toxicity of procaine, are more effective. This has led to an unending stream of new compounds, many of which have recently been reviewed.[2] A paper by Hofmann and Held[3] tabulates references to toxic reactions to most drugs that have been used clinically.

The purpose of this paper is to review the recent literature on this subject and to emphasize the importance of the underlying pathological processes with reference to developing a rational treatment of reactions.

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Many papers have been published on this subject. Steinhaus has pointed out that the problem is difficult to study, first because these reactions are unexpected and second because the number of cases which can be observed by one investigator is comparatively small.

The report of the Mayer committee[4] was one of the early significant studies of clinical reactions. They reported 43 previously unpublished cases of death due to local anæsthetics, almost half of which were due to the injection of cocaine before tonsillectomy. Because of its toxicity, all authorities now condemn the use of cocaine for infiltration purposes. The Mayer report showed that the occurrence of an accident seldom found the operator ready to apply suitable measures promptly. The committee advised artificial respiration and cardiac massage as the most effective methods of treatment for these intoxications.

Not all reactions are serious. It is just as important to look for and recognize the minor toxic manifestations. These act as a warning that further administration of local anæsthetic may lead to more serious symptoms.

### CAUSES OF REACTION

*Psychogenic Influences.*—Apart from the drug used, other influences may act upon the patient. A dread of local anæsthesia resulting from a previous experience, or the anxiety of friends or relatives, leads to tension and nervousness, and

such a state is apt to be accompanied by increased circulating adrenaline. Fainting and even death before the administration of the anæsthetic is not unknown. It is often difficult to separate these neurogenic reactions from those of the local anæsthetic. Preoperative discussion and psychic premedication is a remedy for this reaction. Crampton stressed that "personality is non-toxic and does not throw any strain on the heart, liver or kidneys, nor does it depress respiration".

Local anæsthetic procedures depend upon a general approach to the patient and his problems. Unless the patient is co-operative, other techniques should be seriously considered. It is most unwise to force local anæsthesia on an unwilling subject, and the establishment of the patient's confidence is a matter of prime importance to the success of the anæsthesia.

Gentle handling and quietness in the theatre are other factors to be emphasized.

### ADMINISTRATION HAZARDS

(a) *General condition of patient.*—Excluding the problem of psychomotor reactions, many authors have blamed "hypersensitivity" and "idiosyncrasy", terms often loosely applied and not nearly as common as a true overdose.

Debilitated, aged, or shocked patients are more susceptible to toxic agents, and less concentrated solutions should be used in these poor-risk cases. Albert[5] discusses techniques employing minimum doses of drugs.

(b) *Toxicity of drugs used.*—True assessment of toxicity is difficult, for it is based upon animal experiments which may not be strictly applicable to man. Considerable variation in enzyme patterns from species to species gives rise to different rates of hydrolysis. Little attention has been paid to this aspect of the problem by the pharmacologists investigating these drugs. Tetracaine and dibucaine are considerably more toxic for guinea pigs than for mice, while the reverse is true for procaine.[6] In clinical practice the relative toxicities are further complicated by the fact that the more potent drugs are used at greater dilution. Many factors of practical importance determine the actual toxicity.

(c) *Total weight of drug injected.*—Most textbooks list average doses by weight for each drug, but, as Gillies points out, the speed of absorption is more important than the dose used. Rubin,[7] working with rabbits, administered an intrabronchial dose of tetracaine that produced toxic symptoms when three to four minutes were spent on injection. When the same dose was given in 15 seconds, immediate death resulted. Further experiments with cocaine gave identical results. The importance of the speed of absorption in the etiology of so-called abnormal responses to local anæsthetics must not be underestimated.

(d) *Concentration of solutions.*—The more concentrated solutions are used for blocking large nerve trunks, and the more diluted for skin infiltration. The former are associated with a greater risk should accidental intravascular injection occur.

Ahroon[8] reported a case of a death from tetracaine where the solution labelled 2% was found on analysis to be nearer 6%, due to its being stored in a poorly stoppered bottle and having become concentrated by evaporation.

When ordering solutions, oral messages should not be permitted. Because of the similarity of many names for drugs of widely differing toxicities, misunderstandings similar to that reported recently[9] are not infrequent.

(e) *Sites of injection.*—Different areas have different rates of absorption. This has been demonstrated in guinea pigs by Shumacher by estimating the median lethal dose for procaine by different routes of administration. The most toxic were intravenous and intrapleural (41-42 mg./kg.); absorption by the intramuscular (330 mg./kg.), subcutaneous (410 mg./kg.) and intraperitoneal (750 mg./kg.) routes was slower. It is interesting to note that he was able to demonstrate a difference in the area of paravertebral injection. The lumbar region (250 mg./kg.) was a less toxic route than the thoracic (115 mg./kg.) in paravertebral injection. Batson's study[10] of the vertebral veins may offer an explanation for the latter observation. He was able to demonstrate that the entire system of epidural and vertebral veins has a free and rich anastomosis at each spinal segment with veins of the thoracico-abdominal cavity; when radiopaque medium was injected, it was found to reach the transverse cranial venous sinus and the superior longitudinal sinus. In experiments in living animals, he was further able to show that when the intrathoracic or intra-abdominal pressure was increased, blood flowed into the vertebral pool in preference to entering the vena cava

directly. This route-of absorption, with its direct communication with the large cerebral sinuses, may be a factor in the rapid absorption of drugs injected in the paravertebral region. It is certainly a contributory factor to the reactions reported following topical application to the urethra. Batson has demonstrated that media injected into the veins of the penis passed in preference via the vertebral veins and were noted in the cerebral sinuses. These veins are the main channel for absorption from the subarachnoid space, as Howarth and Cooper[11] demonstrated by using radioactive dibromoprocaine.

It is thus apparent that apart from actual intravascular injection, which can occur anywhere in the body, certain areas, owing to their vascularity and drainage, contribute to the general toxicity of the drugs administered. Such an area is that of the upper respiratory passages and the tracheobronchial tree.

Rubin and Kully[12] have criticized the various procedures for topical anæsthesia of this site in that there is no agreement as to basic considerations such as choice of drug, concentrations and amounts, preliminary testing for sensitivity, method of application and the addition of adrenaline. Cocaine and tetracaine are the two most widely used drugs for this procedure. In many of the reported cases of toxic reactions, only vague references are made to the quantity of the drug used, but even when a strict technique such as is described by Weisel and Tella[13] is followed, toxic reactions are not completely eliminated.

(f) *Addition of epinephrine.*—Braun was the first to advocate the use of epinephrine to prolong the duration of anæsthesia by establishing vasoconstriction. Cocaine is the only local anæsthetic to possess effective vasoconstriction of its own. Minute amounts of epinephrine are sufficient and the optimum concentration is 1:200,000; no further efficiency results from a higher concentration. The practice of adding epinephrine by means of drops is to be condemned,[14] as the size of the dropper can result in variations in the solution up to 200%. Epinephrine should be measured accurately by means of a syringe, for it possesses toxic properties not infrequently confused with those of local anæsthetics; namely, anxiety, nervousness, headache, weariness or palpitation. However, its addition is a bulwark against the too rapid absorption of injected local anæsthetics. The recent report of Ansbro *et al.*[15] illustrates an increased incidence of convulsions following administration of lidocaine without epinephrine in the lumbar epidural region.

Opinions are divided regarding the advisability of adding epinephrine to tetracaine for topical anæsthesia of the tracheobronchial tree,[16] but evidence from animal experiments[7, 17] condemns this practice and claims that it may be a factor increasing the toxicity.

## TYPES OF REACTIONS

The classification and description of local reactions have been summarized by Sadove *et al.*[18] These authors claim that, pharmacologically, one is dealing with overstimulation to the point of depression in all cases of toxic reaction to local anæsthetics. In one and the same case, all types of reaction may be encountered simultaneously to a varying degree or consecutively. Their classification is based upon central-nervous-system effects where stimulation or depression is predominant, and peripheral effects upon the cardiovascular system and respiratory tract. For full discussion, the original paper should be studied.

## SITES OF TOXIC ACTION

### (a) *Central nervous system*

The occurrence of convulsions has prompted research into the effects of local anæsthetics on cerebral tissue. The respiration of brain homogenates and rat-cortex slices has been shown to be depressed by local anæsthetics. The exact site of this depression is not known, but a recent paper suggests that it may be due to inhibition of the synthesis of citrate.[19]

The effect of local anæsthetics on the electrical activity of the brain has not been extensively studied. Toman and Davis[20] report that after intravenous injection of procaine the electroencephalogram of rabbits demonstrated changes essentially similar to those seen after the administration of the stimulant metrazol. There was an increase in threshold for evoked cortical responses, together with repetition and increased voltage and widespread irradiation. These authors suggested that a threshold-raising drug may cause convulsions by selective depression of inhibitory systems.

Much further work is required before the

problem of the mechanism of local anæsthetic convulsions is fully understood.

Clinically, the effects on the central nervous system may be predominantly stimulation or depression.

*Stimulation* depends upon the area affected and may be subjective; namely, a feeling of apprehension, nervousness or nausea. If the motor cortex is involved, convulsions may occur. Treatment is by the administration of minimal doses of a short-acting barbiturate.

*Depression* may supervene after a period of stimulation or, as observed with lidocaine, may precede convulsions.[21] It is interesting to note that Bernhard and Bohm[22] have successfully used intravenous lidocaine in the treatment of epilepsy.

Recent experiments by Maykut and Kalow[23] in guinea pigs with procaine and barbiturates have demonstrated that the hypnotic and convulsive effects of procaine represent two independent actions on the central nervous system. The stimulating convulsant property of the local anæsthetic is counteracted by the barbiturate, but the depressant action appears to augment and is perhaps identical with the lethal action of the barbiturate. From a practical point of view, this would indicate that only the minimum amount of barbiturate, just sufficient to control convulsions, should be administered. Otherwise, the barbiturate will only aggravate any ensuing depression. Convulsions must be controlled, for they lead to irreversible cerebral damage from anoxia.

(b) *Cardiovascular system*

After topical application of local anæsthetics to the heart, Mautz[24] demonstrated a significant rise in the electrical threshold of the heart for premature systoles, but in large doses a weakening of the heart's action. Long *et al.*[25] studied the effect of increasing intravenous doses of procaine on the electrocardiogram in dogs. Doses of 10 mg./kg. caused changes in the amplitude of the E.C.G., and increasing the dose successively produced bundle branch block, some slowing of conduction through the A.V. node, ventricular tachycardia, and ultimately ventricular fibrillation. With the onset of the bundle branch block, the contractile force of the heart decreased. Provided respiration was maintained, cardiac changes short of ventricular fibrillation were found to be reversible. Both ether and barbiturates were used for preliminary anæsthesia, and no difference was noted in the type of electrocardiographic change after intravenous administration of procaine. This indicates that the presence of the barbiturate does not influence the course of the toxic action on the heart. However, no convulsions occurred in the dogs under barbiturate anæsthesia, whereas when ether was the anæsthetic extensor spasms and convulsions were noted. Knoefel *et al.*[26] claim that after intravenous injection the heart, being the first organ to be reached by a massive dose, is the first to fail. This concept would explain the rare occurrence of immediate death following injection.

Treatment of cardiac arrest consists of artificial respiration and institution of cardiac massage. Central depression may manifest itself by peripheral vascular collapse and is treated by means of a vaso-constrictor and administration of intravenous fluids.

## ALLERGY TO LOCAL ANÆSTHETICS

Through frequent contact with local anæsthetics, dentists often develop dermatitis as a result of becoming sensitized to the drug.[27]

Lane and Luikart[28] have reviewed 107 cases from the literature and condemn the current practice of prescribing ointments for topical use for relief of pruritus without consideration of the risks of possible sensitization.

In dental anæsthesia, Mitchell reported two cases of delay in the onset of allergic phenomena. Adler[29] has investigated the specificity of these reactions and demonstrated the presence of strong group specificity. He claims that where allergy to one anæsthetic of the procaine series is present, local anæsthetics with a different chemical structure and not derived from para-aminobenzoic acid can safely be employed.

Criep and Ribeiro[30] recently reported three deaths from allergy to procaine, but this has been criticized[31, 32] and the rarity of true allergy to local anæsthetics emphasized. Only after errors of judgment have been rigidly excluded is such an explanation justifiable.

## SUMMARY

Some hazards associated with the administration of local anæsthetics have been presented and the mechanisms discussed. There must be a clear conception of the various forms in which

a reaction may manifest itself, and an appreciation of the importance of early treatment is essential.

The minimum apparatus for resuscitation must be to hand. This need not be elaborate, but should include means for artificial respiration such as a bag and mask, and facilities for the injection of a short-acting barbiturate.


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# RETICULOSARCOMA OF THE THYROID GLAND (STRUMA RETICULOSA)*

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RETICULOSARCOMA of the thyroid gland refers to an uncommon disease of this organ, which has been reviewed by Brewer and Orr[1] in 1953, and for which they prefer the term struma reticulosa. This terminology is suggested because of an element of doubt regarding the exact nature of the lesion, and these authors suggest that its neoplastic nature in the usual sense is not as yet proven.

Kellett and Sutherland,[2] in 1949, reported upon five cases of primary reticulosarcoma of the thyroid gland, all in elderly women and with four deaths occurring within two years of operation. In two of these cases there was evidence of a malignant recurrence. One case was alive and well two years after postoperative irradiation therapy.

Brewer and Orr[1] detected their cases when reviewing the undifferentiated tumours of the thyroid gland encountered in a large English general hospital, being stimulated to do so because of an unusually long survival in some cases that had been so diagnosed. In a total of 65 cases of malignant thyroid neoplasms, 22 had been diagnosed as undifferentiated tumours. In these, death had ensued in nine out of 10 cases which they found to be carcinomatous. There were two survivors who, upon review, were considered to have had a chronic thyroiditis. They found 10 cases that could be categorized as struma reticulosa, and of these there were four with long-term survival. They point out that in the fatal cases the survival time was very short and never exceeded one year.

In reviewing 47 possible cases of this disease available in the literature, Brewer and Orr[1] found eight instances of survival with freedom from recurrence. They point out that autopsy studies in fatal cases are very few but from these a most unusual distribution of metastases is apparent; namely, a high incidence of occurrence in the gastrointestinal tract. Of nine cases in which post-mortem examination was made, four showed metastases in the gastrointestinal tract and regional lymph nodes only, whereas in another four cases the gastrointestinal tract was included in the metastatic distribution.

It is because of these irregularities of behaviour that Brewer and Orr[1] suggest the possi-

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bility that the process is an unusual granulomatous one with a predilection for the thyroid gland and the intestinal wall. Four out of 10 cases had prolonged survival and some showed a fibrotic healing process, not necessarily attributable to irradiation therapy. They stress the almost complete occurrence in elderly women.

The pathological changes consist in a tumorous-like replacement and enlargement of the thyroid gland produced by a proliferation of reticulum cells intermingled with lymphocytes, the latter cells tending to accumulate at the margins of the tumour areas. In some cases abundant fibrous tissue is also present at the margins or is infiltrated by these cells. The fibrolymphoid margin may be contained within the thyroid gland or may invade the muscles of the neck, often in advance of the more neoplastic reticulum cell proliferation.

Our interest in struma reticulosa was aroused by its recognition in a recent case submitted to a subtotal thyroidectomy. Having become conscious of this condition, we identified it in a second case diagnosed as an undifferentiated small cell carcinoma in 1949, and surviving free of evident recurrence to the time of writing in 1955.

## CASE REPORTS

### CASE 1

Mrs. J.N., age 60, was admitted to the Montreal General Hospital on April 14, 1955. She had been attending the outpatient department for some months with complaints of fatigue, drowsiness, headaches, and a weight loss of 10 lb. The basal metabolic rate and the radioactive iodine uptake showed her to be euthyroid. Her symptoms were not relieved by the administration of thyroid extract. A few weeks before admission, a nodular enlargement of the thyroid became apparent and thyroidectomy was advised.

On examination the pulse rate was 78, the blood pressure 180/108. There was no tremor of the hands or tongue. The thyroid showed a multinodular enlargement involving more especially the right lobe. The trachea was displaced slightly to the left. There was no tenderness over the gland. Because of the hardness of some nodules, the possibility of malignancy was entertained though the voice was normal and there was no fixation of the gland.

At operation on April 18 the thyroid gland was found to be enlarged due to the presence of multiple nodules, the right lobe being larger than the left. While the nodules were almost all of a firm consistency, there was one hard nodule in each lobe.

A subtotal excision of the right lobe was first carried out, leaving behind a residue of firm thyroid tissue on the posterior capsule amounting in volume to about one-quarter of a normal lobe. Grossly this lobe appeared carcinomatous, but examination of frozen sections did not confirm this. The isthmus was then dissected free from the trachea and a subtotal resection of the left lobe performed.

### PATHOLOGY

The specimen of thyroid gland weighs 45 g., being enclosed in an apparently intact, thin, shiny fibrous capsule and being of abnormally pale colour and of firm consistency. It is uniform throughout, with the gland parenchyma replaced by an irregularly lobulated or pseudolobulated, rubbery, firm, grey-white homogeneous tissue, the lobulation being produced by fibrous bands irregularly distributed throughout the mass.

The anatomical appearance at operation suggested thyroid carcinoma, but an immediate impression from frozen section was that of a chronic thyroiditis.

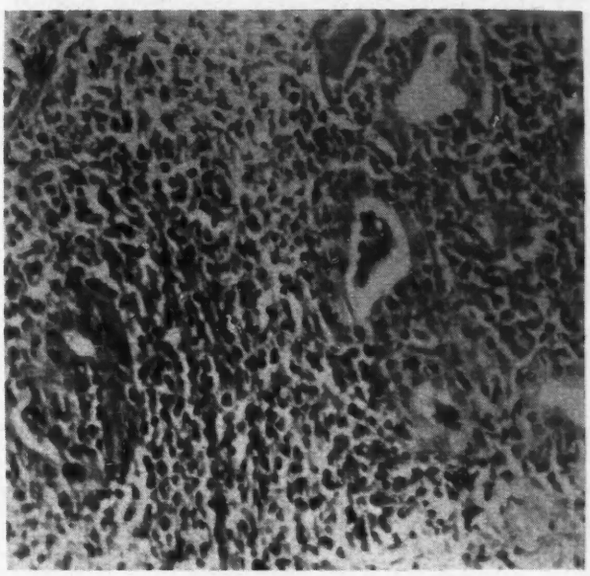

Fig. 1.—Case 1. Cellular tissue that replaces thyroid parenchyma and remnants of acini within it.

Microscopic examination (Fig. 1) reveals some small areas where the thyroid acinar architecture is maintained in a variably atrophic state with small follicles and reduced, little, or no colloid. In some, epithelial atrophy and shrinkage have occurred, while in others the epithelium remains fairly tall and well preserved. In these areas small lymphoid cell nodules are present but the epithelial, large acidophilic cell features of lymphadenoid goitre are not noted. Much of the parenchyma has been replaced, with only scattered, more or less isolated, shrunken and atrophic acini or epithelial remnants in a widespread proliferative process, much of which consists of bands and sheets of anastomosing fibrous tissue that enclose a cellular tissue occurring as minute islands, larger

nodular foci and in some places as broad sheets. This cellular tissue sometimes infiltrates in partly preserved thyroid parenchyma, or encloses remnants indicating replacement by it; whereas it in turn is enveloped in the abundant proliferation of fibrous tissue which sometimes appears to be encroaching upon the cellular tissue and replacing it.

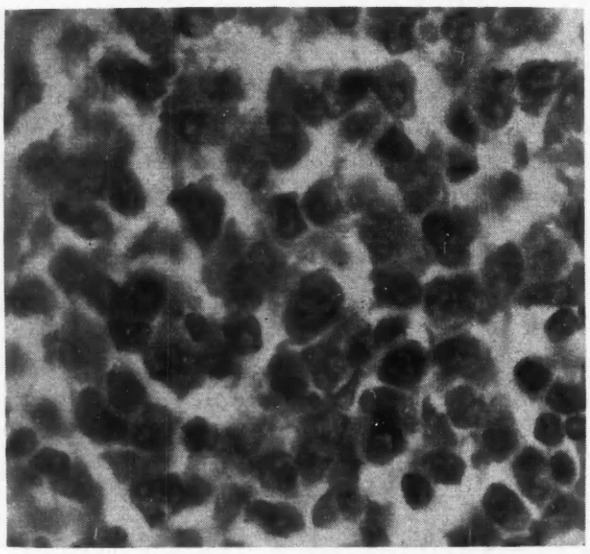

Fig. 2.—Case 1. Appearance of the dominant reticulum cell proliferation. Occasional lymphocytes are intermingled.

The cellular tissue (Fig. 2) is formed largely by a syncytial meshwork of cells of moderate size, irregular or ill-defined shape, having quite abundant, pale, acidophilic, non-granular cytoplasm, and relatively large, rounded, irregular or reniform nuclei with quite abundant pale nucleoplasm, a rather prominent acidophilic nucleolus and a variable condensation of chromatin at the nuclear membrane. They are interspersed by not infrequent smaller mononuclear cells resembling lymphoblasts or even lymphocytes. There are scattered mitoses, and occasionally it becomes difficult to distinguish the acinar epithelial remnants from the dominant larger reticulum cell. There is a very faint, delicate, reticular fibrillar stroma in the cellular masses, and within them there occur scattered lymphoid cell foci. Sometimes the lymphoid cells predominate at the margins of the reticulum cell proliferation.

The pathological diagnosis is reticulosarcoma.

CASE 2

Miss C.B., age 50, presented herself in March 1949 with complaints of nervousness, palpitation and weakness for two months, and a weight loss of 20 lb. in three months. A radical mastectomy had been performed in Toronto in 1947 for carcinoma of the left breast. This was followed by a course of x-ray therapy.

On examination it was found that she had a marked fine tremor of the outstretched fingers, a definite quadriceps weakness, and pulse rate of 102. Her blood pressure was 146/78. There was a generalized, very firm enlargement of the thyroid. No bruit was heard over the gland, which was not fixed. The basal metabolic rate (B.M.R.) was found to be +42.

Though there was some tenderness over the right lobe of the thyroid, the signs and symptoms of hyperthyroidism seemed too pronounced for thyroiditis, and a diagnosis of diffuse toxic goitre was made. Lugol's iodine was prescribed in a dosage of five drops three times a day.

She was admitted to the Montreal General Hospital on April 8, 1949. At this time she showed a remarkable clinical improvement, the B.M.R. having fallen to +4, and the pulse rate to 64.

At operation on April 13, the thyroid gland was found to be diffusely enlarged and very firm. Because of the unusual firmness a small portion of the right lobe was excised for immediate microscopic examination. The cut surface of the gland showed a solid tissue of whitish colour. The pathologist reported this to be a small cell carcinoma.

The right lobe of the thyroid was completely excised, the recurrent laryngeal nerve being sacrificed since this ran inside the gland capsule. The isthmus and pyramidal lobe were then removed and a subtotal excision of the left lobe carried out, leaving behind a small amount of gland tissue on the posterior capsule so as not to endanger the parathyroids. As the cut surface of the remaining thyroid tissue had a white, firm appearance similar to that of the right lobe, it was felt that even with this extensive excision the carcinomatous tissue had not been completely removed.

After operation there was some voice change associated with the paralysis of the right vocal cord. A full course of x-ray therapy was administered. With the oral administration of thyroid extract, she remained quite well until March 1950 when a firm mass 4 cm. in diameter was found in the right breast. A radical mastectomy was performed and the pathologist reported a sclerosing carcinoma simplex with no evidence of axillary node metastases. During the past five years she has had periodic follow-up examinations including x-ray surveys of the chest and skeleton. No evidence has been found of any recurrence of malignant disease, and her general health remains good.

This case was of considerable interest to the authors because the patient had had three primary malignant tumours, with an eight-year survival following operation for carcinoma of the left breast, a six-year survival after carcinoma of the thyroid and a five-year survival after carcinoma of the right breast.

However, since individuals with anaplastic carcinoma of the thyroid almost invariably die within a few months, the long survival in this case stimulated a review of the microscopic sections and the diagnosis has now been revised.

PATHOLOGY

A total weight of 35 g. of tissue was resected in a subtotal thyroidectomy and contains a calcified adenomatous nodule within the lower pole of the left lobe. The gland tissue, particularly in the right lobe, is firm and pale and partly interrupted by visible fibrous bands. An immediate frozen section was interpreted as indicating an anaplastic small cell carcinoma and the original

pathological diagnosis made was diffuse small cell carcinoma of the thyroid gland with associated lymphoid hyperplasia and a solitary calcified adenoma. This occurrence of lymphoid hyperplasia in thyroid carcinoma was remarked upon as being unusual.

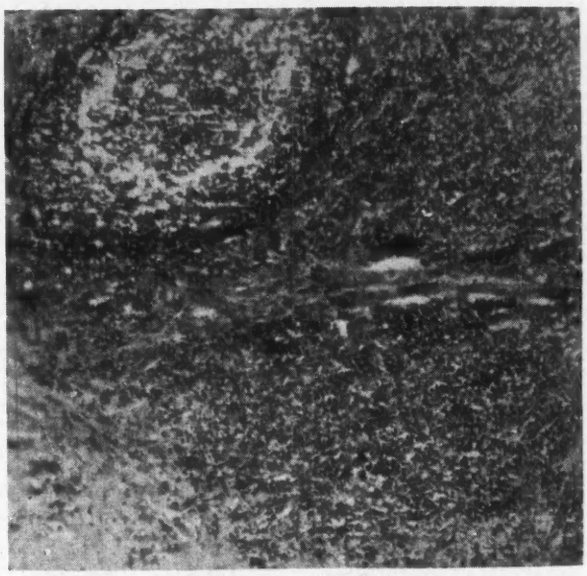

Fig. 3.—Case 2. Diffuse cellular tissue replacing thyroid parenchyma with one lymphoid follicle and thin fibrous bands present.

Upon review of the microscopic sections (Fig. 3), it is apparent that the original diagnosis was not correct. The thyroid parenchyma is widely replaced but does contain several small atrophic colloid follicular nodules demarcated by connective tissue capsules and in areas reveals shrunken lobules formed by markedly shrunken and atrophic thyroid acini. Wide areas, however, are replaced by a cellular proliferation of mildly pleomorphic reticular cell type, remarkably like that described in greater detail in Case 1. Here, too, some lymphoblast-like or lymphocytic cells are interspersed and there are well-defined, scattered lymphoid follicles with wide germinal centres. Such areas occur in small and larger nodules or islands or in broad sheets, marginally demarcated by scanty or marked fibrous tissue proliferation. There are areas where the dense fibrous tissue predominates. Frequently, acinar remnants are present in the areas of cellular proliferation. The amended diagnosis is reticulosarcoma of the thyroid gland.

## DISCUSSION

The clinical and pathological features of two cases of an unusual condition, reticulosarcoma of the thyroid gland, are described. One of these patients is free of apparent recurrence six years after thyroidectomy and postoperative irradiation, a survival that is not consistent with the original diagnosis of an anaplastic small cell carcinoma of the thyroid gland. It is evident from the literature that this error in diagnosis has been repeatedly made in other cases of this disease. The clinical, operative and gross pathological features of reticulosarcoma of the thyroid gland resemble those of carcinoma, lymphadenoid goitre, or chronic thyroiditis. In our present relative ignorance of the nature of this condition it would seem well to consider it a malignant lymphoma, rather than a granulomatous process as has been suggested.

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## MEDICAL PROBLEMS OF SKIN DIVING

The increasing interest in skin diving and the increasing number of accidents and fatalities associated with it have led Dr. W. T. Burns of California to publish a most instructive article on its medical problems.

There is need for some general enlightenment of physicians, since the problems posed are of an unusual nature, usually in the past only encountered by those associated with deep sea diving operations. Dr. Burns discusses the apparatus used by skin divers and gives some general comments on the physics and physiology of diving. He warns would-be divers that perfect health is essential. The ideal type of diver is young, slender and cool-headed. Obesity is a definite hazard because fat tends to retain nitrogen and also because fat persons are more readily exhausted. Any type of chronic illness may prove disastrous to a diver, and nervousness and panic are obviously conducive to catastrophe. The circulatory retardation associated with smoking and the consumption of alcohol can also be dangerous. Head colds are particularly detrimental in diving, and rupture of the eardrums may rapidly ensue.

The five conditions which may lead to disaster are listed as: caisson disease, air embolism, asphyxia, carbon monoxide poisoning and oxygen poisoning. Caisson disease with the usual signs of pain in the chest calls for sedation and recompression where a suitable chamber is available. Air embolism, associated with shock, vomiting, paralysis and coma requires sedation, treatment for shock, artificial respiration, oxygen inhalation and recompression. Asphyxia does not differ in signs and symptoms from that due to other causes. In carbon monoxide poisoning the usual measures of artificial respiration, oxygen inhalation and anti-shock treatment are needed. Oxygen poisoning causes nausea, bronchial irritation, dizziness, muscle twitching and emotional disturbances; sedation and anti-spasmodics are necessary.—W. T. Burns, *J. A. M. A.*, 159: 5, 1955.

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# LIPOMELANIC RETICULOSIS*
## (DERMATOPATHIC LYMPHADENITIS)

ROBERT JACKSON, M.D., *Regina, Sask.*

MANY PATIENTS with an extensive dermatitis of varying types (e.g., psoriasis, lichen planus, contact dermatitis, or atopic dermatitis) develop a widespread superficial lymphadenopathy. A small proportion of these cases occur in patients who have a malignant lymphoma; however, in most cases the process is completely benign. In recent years careful study of a number of these benign cases[3, 5, 7] has revealed that the lymph nodes often show a specific histological picture. This condition has been called lipomelanic reticulosis (dermatopathic lymphadenitis). It is secondary to the extensive skin eruption. When the skin eruption decreases or disappears, these lymph node changes may do likewise. Lipomelanic reticulosis is not a malignant lymphoma, although it has been so considered in the past owing to its similarity to Brill-Symmers's disease, Hodgkin's disease and other lymphomas. The pathogenesis is unknown.

The histological picture in the nodes is characterized by large, pale cortical areas which have deposits of melanin in their periphery. These areas are composed of reticular cells, the cytoplasm of which contains cholesterol. There is also a polymorphous cell infiltrate.[3]

The histological findings in the skin are usually those of a non-specific dermatitis, although some may show features of the primary skin disease.

In a recent paper[3] this condition was extensively reviewed and six additional cases were presented. At that time an intensive search of the literature revealed only seven reports of post-mortem examinations on patients who had lipomelanic reticulosis.[1, 2, 4, 6] Since then one more has been added.[7]

### CASE REPORT

A 60-year-old Hungarian male was admitted to the Montreal General Hospital on August 23, 1954. He gave a three-week history of an extensive dermatitis which started on his right hand and spread rapidly to other parts of his body; he had been applying an ointment, the nature of which could not be determined. He had had an "itchy rash" in 1922. Functional inquiry and personal history revealed nothing of significance as regards his skin condition. He had no gastrointestinal complaints.

The patient was a moderately well-developed and well-nourished white male, weighing 139 lb., with a generalized exfoliative dermatitis or erythroderma. On closer examination, small guttate psoriatic lesions were visible; these were most easily seen on his trunk. There was some weeping about the wrists and on both lower legs, and some loss of hair from his axillæ, eyebrows and scalp. Axillary, cervical and inguinal lymph nodes were enlarged to the size of small grapes. They were neither fixed nor tender. The blood pressure was 110/70, and the pulse 90, with occasional extrasystoles, and some cardiac enlargement to the left. The patient was edentulous. No further abnormalities were demonstrated.

Urinalysis showed an occasional white cell on three occasions and an occasional red cell on one occasion. The V.D.R.L. exclusion test was negative. The fasting blood sugar was 125 mg. %. The red cell count was 4,600,000, hæmoglobin value 88%, white cell count 7,500 with 67% neutrophils, 24% lymphocytes, 3% monocytes and 6% eosinophils. The electrocardiogram revealed auricular extrasystoles. A roentgenogram of the chest showed cardiac enlargement. The Wassermann reaction on spinal fluid was negative. Two biopsies of the skin showed parakeratosis with micro-abscesses, acanthosis with some elongation and clubbing of the rete pegs, some thinning of the supra-papillary epidermis and an inflammatory process in the papillæ and upper corium. No pigment granules were seen. These sections were considered to be suggestive of psoriasis. Examination of an excised axillary lymph node showed the characteristic features of lipomelanic reticulosis, as outlined above (Figs. 1 and 2). A silver stain for melanin

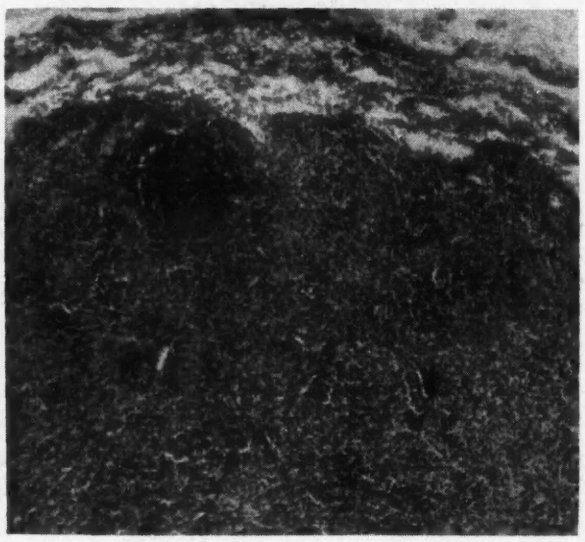

**Fig. 1.**—Axillary lymph node in lipomelanic reticulosis. Note atrophic follicle and replacement of normal node architecture by masses of reticular cells. Hæmatoxylin and eosin stain. 60 × (approx.)

was positive. The Prussian blue reaction for hæmosiderin was negative.

The patient was first put on a bland routine consisting of wet saline dressings and oatmeal baths. Later quarter-strength Ung. Picis Co. was used with marked improvement of his eruption. He died very suddenly on September 27. The clinical diagnosis was psoriatic erythroderma with lipomelanic reticulosis of axillary lymph nodes, and cardiac enlargement with auricular extrasystoles.

Post-mortem examination* showed massive pulmonary embolus; silent ulcerative adeno-

*From the Department of Dermatology, Montreal General Hospital, R. R. Forsey, M.D., F.R.C.P.[C.], Chairman, with whose kind permission this case is reported.

*Courtesy of Dr. W. H. Mathews, Associate Pathologist, Montreal General Hospital.

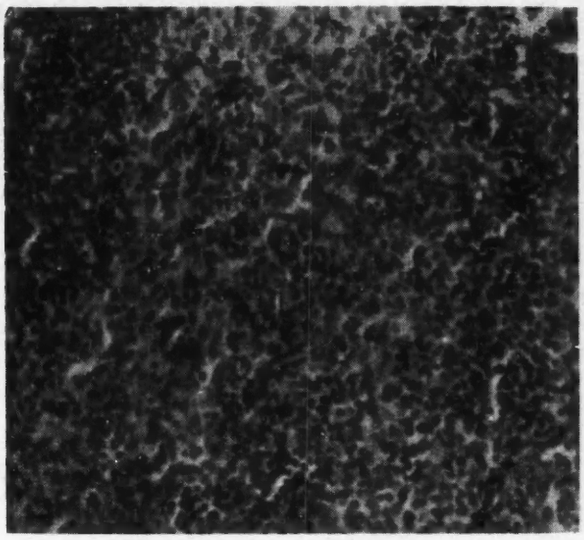

Fig. 2.—Axillary lymph node in lipomelanic reticulosis. Note large number of pale reticular cells with interspersed lymphocytes. Hæmatoxylin and eosin stain. 240 × (approx.)

carcinoma of the stomach, lesser curvature, without evident perigastric extension or metastases; dermatitis, probably psoriasis, widespread; lipomelanic reticulosis (dermatopathic lymphadenitis), axillary, inguinal and about the common iliac vessels. There were a number of associated conditions of no special interest.

The source of the pulmonary embolus was not found, even though the lower limb veins were explored.

Silver staining of one of the involved nodes for melanin was positive. The Prussian blue reaction for hæmosiderin was negative. Sudan III staining revealed many small fat droplets in some of the reticular cells. Lymph nodes showed no evidence of lipomelanic reticulosis in the following locations: over the left internal jugular vein, in the greater omentum, about the abdominal aorta, beside the œsophagus, at the bifurcation of the trachea, from both hilar regions, from the mediastinum and from the portal area. The liver, spleen and other visceral organs showed no evidence of lipomelanic reticulosis.

## COMMENT

The nodes about the common iliac vessels could have been involved by any or all of the following routes: via the deep lymphatics from the lower limbs, via the lymphatics from the lower abdominal wall, or by extension of the process from the inguinal nodes.

## SUMMARY

A case of psoriatic erythroderma with lipomelanic reticulosis is presented. This is the ninth reported case which includes the results of a post-mortem examination.

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# STAPHYLOCOCCAL ENDOCARDITIS*

ANDREW KELEN, M.D. and
M. R. STALKER, M.D., *Ormstown, Que.*

AT THE PRESENT TIME staphylococcal septicæmia has a mortality of 50% and the majority of deaths are due to the presence of acute endocarditis.[1] The following case illustrates this point.

A.T., a 35-year-old French Canadian truck driver, developed a small boil on the left elbow which he pricked with a needle. Within a few days he developed high fever, malaise and respiratory difficulty. He was admitted to hospital on September 28, 1954, with a cellulitis about the elbow and septicæmia. Blood cultures revealed staphylococci in large numbers which were sensitive to chloramphenicol, erythromycin and bacitracin.

Accordingly he was given erythromycin 2.4 g. and chloramphenicol 2 g. daily. In addition staphylococcal antitoxin was given. A radiograph of the chest revealed multiple small circular shadows which were interpreted as lung abscesses.

During the 10 days after admission he improved clinically, but cultures of the sputum and pleural fluid showed the continued presence of staphylococci. After 17 days chloramphenicol was discontinued for fear of its potential toxic effects and as there appeared to be

*From the Barrie Memorial Hospital and the Ormstown Medical Centre, Ormstown, Que.

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sufficient general improvement in the patient's condition. A radiograph indicated that the process in the lungs was subsiding.

Shortly afterwards the patient's condition deteriorated. Blood cultures showed that staphylococci were still present. The organisms were found to be still sensitive to bacitracin and chloramphenicol but becoming resistant to erythromycin. Bacitracin 80,000 units was then given intramuscularly daily for four days. During this time the patient's temperature increased from about 101 to 105° F. and he became even more ill. Urinalyses, previously negative, now showed the presence of red cells and casts. The blood urea nitrogen level rose from 17.4 to 22.7 mg. %. Bacitracin was stopped as it was not helping the patient and was possibly causing kidney damage.

During the fifth week in hospital the patient developed a pericardial friction rub which persisted several days. Petechiæ were noted a few days later over the face, arms and trunk. At no time was a murmur heard. Pneumothorax was another complication.

Blood cultures remained positive, and chloramphenicol was given again, at first 2 g. daily and later 4 g. Erythromycin was stopped when sensitivity tests showed that it was no longer effective.

The patient's condition continued to deteriorate and he died on November 12, some 50 days after the onset of his illness.

Post-mortem examination revealed firmly adherent thrombi on the atrial aspects of the leaflets of the mitral valve. Septic infarcts were present in the kidneys and spleen. The lungs were almost completely collapsed, with innumerable firm fibrinous strands stretching to the chest wall around all sides. There was no evidence of infarction or abscesses in the lungs.

In view of the high mortality from staphylococcal septicæmia the potential toxicity of chloramphenicol should have been disregarded in the treatment of this case. It is possible that the patient's life might have been saved if chloramphenicol had been continued.

The assistance of the Department of Pathology and Bacteriology of the Montreal General Hospital is gratefully acknowledged.

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# MENINGITIS COMPLICATING ADDISON'S DISEASE*

ANDREW KELEN, M.D.,
J. A. DAVIDSON, M.D.,
M. R. STALKER, M.D. and
G. L. SUTTON, M.D., *Ormstown, Que.*

IN ADDISON'S DISEASE even trivial infections may lead to a crisis and are a potential threat to life. This has been emphasized in the published reports of Addisonians with infections such as dental abscess,[1] tonsillitis,[2] pneumonia[3] and appendicitis.[4] Meningitis must be an uncommon complication, as no references were found in the literature.

Our patient with Addison's disease developed appendicitis and a year later meningitis.

P.T., a French Canadian of 29, was first admitted in May 1953, when the diagnosis of Addison's disease was made. He had lost weight and strength, his complexion had become dark, and for five years he had had a productive cough. There was a strong family history of tuberculosis. On examination his blood pressure was 85/56 mm. Hg, he was weak and emaciated, and there was a marked pigmentation of the face, hands, gums and the mucosa of the lips. The Kepler water test was positive. A radiograph showed pulmonary tuberculosis, probably inactive.

The patient was given desoxycortisone acetate (DCA) 2 mg. and sodium chloride 6 g. daily. He gained 10 lb. in 10 days and was dismissed on this regimen much improved. The blood pressure at the time of dismissal was 94/48.

Some two weeks later, on June 2, 1953, he returned with abdominal pain and vomiting which had been present 18 hours. On examination his temperature was 104° F., his blood pressure 110/46. There was marked tenderness in the right lower quadrant. A diagnosis of acute appendicitis with peritonitis was made. He was given DCA 5 mg. and cortisone 250 mg. by the intramuscular route and saline and glucose intravenously. Antibiotics were given before operation, and a markedly inflamed and gangrenous appendix was removed. After operation cortisone, DCA and salt were given and the postoperative course was uneventful. Cortisone was gradually stopped and DCA was decreased. At the time of dismissal he was receiving 3 mg. of DCA daily.

Several months later three pellets of DCA were implanted subcutaneously. He was advised to return for re-evaluation but did not, and he was not seen again till November 10, 1954. Four days previously, he had in succession a sore throat, a severe headache, and a painful right ear. On admission he was weak but not very ill and he had a slight fever. The blood pressure was 110/70. There was evidence of acute tonsillitis, pharyngitis and purulent otitis media. He was given penicillin and 300 mg. of cortisone.

About eight hours after admission he became irrational and his temperature rose to 103° F. He complained of a severe headache. He now had a stiff neck and a positive Kernig sign. The cerebrospinal fluid was found to be turbid and Gram-positive cocci were seen on direct smear. His blood pressure did not drop. Cortisone was given intramuscularly (200 mg.) and by mouth (300 mg. in divided doses). Intravenous fluids containing one million units of penicillin and 2.5 g. of sulfadiazine per litre were given. The patient responded to treatment, and in three days he was again rational. A week later he was well and the cerebrospinal fluid was normal. Cortisone was given in decreasing amounts. Convalescence was uneventful except for one episode of renal colic and hæmaturia attributed to sulfadiazine crystals. The Kepler water test was repeated on November 23 and found to be positive. More DCA pellets were implanted before dismissal, at which time his blood pressure was 108/60.

*From the Barrie Memorial Hospital and the Ormstown Medical Centre, Ormstown, Que.

This patient had relatively little resistance to infection. This has been noted in the published reports. However, there was no evidence of an actual "crisis" in this case, with either of the two complications, which is evidence that the steroid therapy was probably adequate.

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## A METHOD OF MAINTAINING THE LATERAL POSITION*

HAROLD T. DAVENPORT, M.B., F.F.A.R.C.S., *Montreal*

IT HAS BEEN SAID that the full lateral position is perhaps the most difficult in which to keep a patient fixed during an operation.

The continued use of the lateral position during operations on the kidney and sympathetic chain, and the more common use of this lateral position during all forms of chest surgery, make solution of the problem necessary.

Numerous methods are advised but none has been universally adopted as being ideal.

For this purpose the simple device illustrated has been found very satisfactory over a period of more than a year at the Montreal General Hospital.

Several advantages have been gained by the routine use of this method of support. The necessary apparatus (a long lateral brace and a length of one-inch wide metal, both padded) is readily available and can be attached to the side runners of a standard operating table. The fixation so provided is easy to arrange with a minimum of manipulation of the unconscious patient. The device does not obstruct the surgeon or his assistants in any manner. Excess pressure upon the supragluteal region can lead to no major injury as no vital structure is compressed. There is no extra embarrassment of the chest or abdominal movements. By rotation of the pelvis the space between the rib margin and iliac crest can be increased with a small "break" of the tables. The upper shoulder can be moved as desired by the surgeon or by lateral table tilt. A steep Trendelenburg position can be adopted without the patient's sliding cephalad.

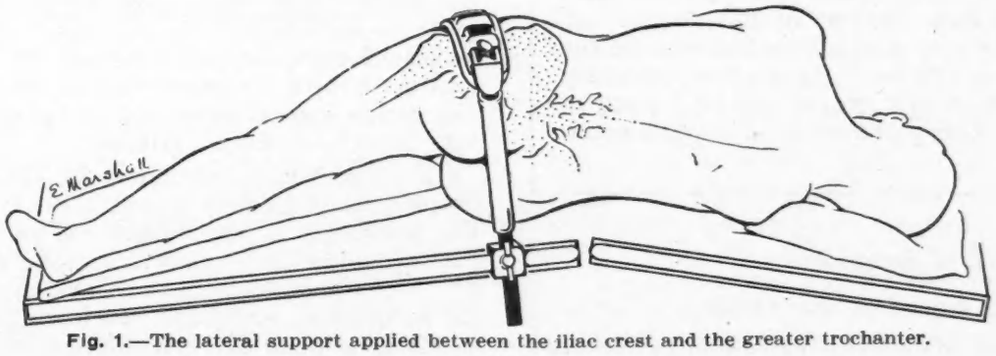


Fig. 1.—The lateral support applied between the iliac crest and the greater trochanter.

Fig. 2.—Patient prepared for an operation upon the right chest—note the lower leg flexed to a right angle.

*From the Department of Anæsthesia, the Montreal General Hospital.

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IMPORTANT NOTICE

It has already been announced that the Canadian Medical Association has purchased a large house at 150 St. George Street, Toronto, in which to consolidate all its activities. Readers of this Journal are asked to note that all departments of the Canadian Medical Association including the staff of this Journal will be housed at *150 St. George Street* from November 21.

## *Editorial Comments*

### HOSPITAL FUNCTION AND DESIGN

With the tremendous expansion of hospitals in Canada during the last decade a great deal of attention has been focused by the medical and nursing profession on the design of the modern hospital in relation to its function. In Britain the Nuffield Provincial Hospitals Trust have also been giving this their attention, and their recently published book on the functions and designs of hospitals* is an excellent survey of present-day thinking on this subject, although unfortunately it makes no recommendations.

With the advent of the four-bed ward and the institution of the nursing team, there has been a wide divergence of opinion as to the optimum size of the ward and nursing unit. The Nuffield Trust's experiments show that the 12- to 16-bed ward may well be the most efficient type and furthermore that no nursing unit should exceed 32 beds. The institution of the treatment room within each nursing unit has probably done much to lessen the burden of the already overworked nurse, and at the same time has greatly minimized the risk of cross-infection. There is no doubt that the treatment room should be an integral part of all nursing units, medical as well as surgical.

Leaving aside the functional and technical design of the modern hospital, probably one of the most radical changes made in recent years has been the great interest in the use of colour in the modern ward. The days of the drab brown and grey walls of the ward have fortunately gone and there is no doubting the effect which pleasant pastel walls and ceilings have on the well-being of the patient—even the psychiatrist will admit that. We must be careful, however, that we do not get carried away with all this, and find our wards with red ceilings and green walls; pleasant, bright, but conservative colours only must be used.

As with the proper use of colour, a great deal can be done to increase the well-being of the patient by the effective use of lighting. Indirect lighting in the ward is essential, but one wonders if in this modern age we tend to overuse fluorescent lights; surely the old-fashioned incandescent light is more pleasing. As far as the patient's bedside light is concerned, apparently no manufacturer has yet come up with the right answer. A fortune certainly awaits the man who can design a good functional and pleasant bedside lamp for the ward patient.

The elimination of noise in the modern hospital has also done a great deal to improve the well-being of the patient. As the Nuffield Trust inquirers have shown, acoustic tiles have not been found to harbour bacteria, and their use is therefore advocated. Much has been done to eliminate noise by using effective floor covering—one wonders however whether the most effective is not the linoleum which has been evolved in the last few decades, with special impregnation and the use of colour.

The Nuffield Trust's report draws attention to the value of a central sterile supply room and a recovery room. It is strange to read that the central sterile supply room is still in the experimental stage in Britain. In North America a central sterile supply area is considered essential in the modern hospital to minimize the risk of infection and at the same time to economize in nursing time.

As regards a recovery room attached to a group of operating theatres, there is no doubt that the setting up of such an area for immediate postoperative cases is one of the greatest advances made in the postwar era affecting surgical technique. In addition the concentration of postoperative cases in one area has improved nursing care and reduced the number of nursing hours in these cases. Its institution however would never have been possible had not great strides been made in recent years in the training of anæsthetists; surely Canada must lead the

*Studies in the Functions and Design of Hospitals. The Report of an Investigation sponsored by the Nuffield Provincial Hospitals Trust and the University of Bristol, England. 192 pp. Illust. $9.50. Oxford University Press, London and Toronto, 1955.

field in this, and the results of the hard labours of our senior anæsthetists are now reaping benefits.

In modern design, therefore, the hospital is gradually being evolved into a bright, cheerful, pleasant building: disappearing rapidly are the gaunt gray and cheerless wards. Everything must be done to continue this trend as we expand our hospitals. At the same time design must be such as to ensure wherever possible the elimination of all unnecessary work for the already overburdened nurse, and get her back to where she belongs—at the patient's bedside.

We must also do all we can in designing the modern hospital to minimize the risk of cross-infection and reduce the risk of postoperative infection. With the advent of antibiotics we tend to overlook this risk to the hospitalized patient. Hospitals and the medical profession would do well to review these matters and not be lulled into a state of false security.

W.S.

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## NEW ORAL DRUG FOR DIABETES

The quest for an orally effective substitute for insulin in diabetes has been a uniformly disappointing one. Physicians will therefore view with caution the claims, advanced last month by German clinicians, to have at last found a safe and reliable, orally effective antidiabetic drug. Nevertheless, the preliminary reports in the *Deutsche medizinische Wochenschrift* sound promising enough to encourage further study of the drug in question.

Franke and Fuchs[1] of Berlin explain that while trying out a new sulfonamide—BZ 55* or $N_1$-sulfanilyl-$N_2$-*n*. butylcarbamide — they noticed that it produced hypoglycæmic symptoms (sweating, hunger, tremor, euphoria) in research subjects. The drug, which gives a high sulfonamide level in the blood even on low dosage, with a maximum level in three hours falling slowly after seven, was found to lower blood sugar level in proportion to its serum concentration, and was therefore tried out in 50 diabetics over a period of a year. Therapeutic results in terms of abolition of glycosuria and lowering of blood sugar level were obtained in 80% of cases of mild to moderate severity. Severe hypoglycæmic reactions never occurred, and the drug was of no use when given intravenously.

Bertram and his colleagues[2] of Hamburg also studied the use of BZ 55 in 82 diabetics, first in hospital and later—after stabilization—as outpatients. They used a more rigid dosage than Franke and Fuchs. Whereas the former stress individual dosage, with three doses of 1 g. each day at first and then 1-1.5 g. a day for maintenance, the latter usually gave 2.5 g. (in 0.5 g. tablets by mouth) on the first day, then 1.5 g. on the second, and later 2 x 0.5 g. daily, regardless of the duration and severity of the diabetes, the body weight or the absorption conditions. In the great majority of cases a therapeutic level was achieved.

The most important findings by this group are that BZ 55 is of no use in young diabetics, in acidosis, or in diabetes complicated by acute infection. In older patients (over 40) with a diabetic history of less than 10 years and a period of insulin therapy under one year, however, the drug produced remarkable therapeutic effects in a high percentage of cases. Thus it stabilized the blood sugar at normal levels in all but three out of 28 older patients who had had diabetes treated dietetically (and unsatisfactorily) for up to 14 years. The effect began on the second to fifth day, and fasting blood sugar levels fell from 300 to 150 mg. %. BZ 55 satisfactorily replaced insulin in 28 out of 38 insulin-treated patients.

It is not yet clear whether continuous therapy is really necessary, for in some cases a 10-day course was enough to stabilize the patient for up to four months on a diet alone in both the above groups, and patients whose conditions had deteriorated without the drug responded again to a second course. Nor did the use of BZ 55 render the patient resistant to insulin. The renal threshold for sugar was not raised.

No intolerance was seen to the drug, which incidentally is a good anti-infective drug, and side-effects are limited to an occasional dermatitis. Achelis and Hardebeck[3] of Mannheim, who discuss the pharmacology of the drug in detail, mention that very high doses in animals cause hyperglycæmia in place of hypoglycæmia, and that the acute toxicity in mice is 11.5 g. per kg., while 1 g. per kg. in rats on chronic administration caused only loss of weight.

Animal experiments and one autopsy result suggest that the drug acts by suppressing function of the alpha cells in the pancreas, thus lowering production of the anti-insulin factor, glucagon.

All three groups of workers are actively engaged in further study of this drug, and urge investigation by others. Further results will be awaited with great interest.

*Prepared by C. F. Boehringer & Sons, Mannheim-Waldhof, West Germany.

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## ANTICOAGULANTS AND GOUT

In the past decade there has been a reawakening of interest in gout. This time-honoured disease seems to have undergone a subtle change in its clinical picture over the centuries, and today is more protean in its manifestations. Biochemical research has placed new methods of rational treatment at our disposal, though it has not as yet solved the riddle of the metabolic error or the reason for the specificity of colchicine in relieving the symptoms in gout. All cases with the clinical manifestations of gout are found to have a high serum uric acid level. Widely differing drugs such as the salicylates, cincophen, probenecid, phenylbutazone, and cortisone increase the excretion of urate by impairing its active reabsorption by the tubules and are called uricosuric agents. The use of these uricosuric agents is becoming established in the treatment of gout.

Sougin-Mibashan and Horwitz in a recent paper (*Lancet*, 1: 1191, 1955) describe the astounding discovery that an anticoagulant, ethyl biscoumacetate (Tromexan), a synthetic coumarin derivative, possesses a uricosuric activity equal to that of probenecid. Their careful experimental work in man and in dogs gives conclusive evidence that ethyl biscoumacetate is a potent uricosuric agent. In the Dalamatian hound, which has a reversed tubular transport mechanism for urate, with active secretion in addition to glomerular filtration, ethyl biscoumacetate, like probenecid, reduces the abnormally large urate clearance. In man, ethyl biscoumacetate produces an impressive rise in the urate clearance and in the urate/creatinine ratio in both normal and gouty subjects. The authors found no clear correlation between prothrombin activity and the fall in the serum urate level.

The authors attempt to find a relationship between the uricosuric, anticoagulant and antirheumatic drugs, but our present knowledge is incomplete, so that their attempt is highly speculative but stimulating. They draw attention to the fact that antirheumatic or antiphlogistic drugs such as salicylates, cincophen, cortisone and phenylbutazone are at the same time uricosuric agents.

"Modification of a metabolic process by a chemical compound is always interesting. When, as in the present case, the observation implicates such widely separated topics as blood coagulation, the biochemistry of gout, coronary atherosclerosis, hepatic and renal function, and the mechanisms of rheumatic inflammation, the scope for further research and correlation is unusually wide."

The interesting clinical application of this discovery may well be in the treatment of myocardial infarction with anticoagulants. This therapy is at the moment controlled in terms of lowered prothrombin time, and the improved clinical results obtained are attributed to this factor. However, Gertler and White[1] have recently shown that coronary artery disease in adults under 40 years is associated with a significantly higher serum urate level than normal. Could it not be that correction of this hyperuricæmia also contributes to the improved results of myocardial infarction treated with anticoagulants of the coumarin series? Not all coumarin derivatives are anticoagulants and it may be possible to produce one with the uricosuric action but lacking anticoagulant properties. A stimulating thought is that it might also possess antiphlogistic properties and so be an added advantage in the treatment of gout.

The paper from Cape Town is a piece of excellent research and poses more questions than it answers. It is hoped that in time when these are answered they will provide a more complete understanding of cellular function in both the kidney and the liver. B.S.

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## SILICOSIS IN ONTARIO

An analysis by N. F. Parkinson[2] of the available records in Ontario has yielded some valuable information on silicosis in this province. The task has been complicated by the wide annual fluctuation in the size of the labour force exposed to silica dust, and the difficulty of following up those who have left the industry, and also by the fact that today a much longer period of exposure is required to produce the disease. Ontario legislation to control the pneumoconioses dates substantially from 1926 when silicosis was first made an industrial disease for compensation purposes. This was followed in 1928 by an enactment providing for compulsory preemployment chest x-ray examination and a mandatory annual medical certification for employment in occupations involving a dust hazard. Dust extraction and suppression together with improved mine ventilation have been employed for the past 25 years, and from 1944 onwards aluminium powder has been used prophylactically in Ontario gold mines. These measures have produced a gratifying improvement in morbidity and mortality statistics.

Contrary to popular belief, experience in Ontario shows that the development of silicosis does not at present appreciably decrease life expectancy, although it does occasionally contribute to the early death of an affected person. Tuberculosis continues to be the most disabling

factor and is the chief cause of death in silicosis. It is noted that many silicotics are able nowadays to continue in gainful employment, often in their usual occupation. During the past quarter of a century the average recorded age of development of the condition has risen from 41 to 56 years and in like manner the average period of dust exposure required for clinical precipitation of the malady has been extended from 15 to 25 years. Perhaps, however, the most encouraging fact to emerge is that only 45 cases of silicosis (less than 4% of known cases) have occurred amongst those who have entered the mining industry since 1928.

J. D. MEDHURST

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## STATEMENT RE PRESENT STATUS OF POLIOMYELITIS VACCINE

FROM THE DEPARTMENT OF NATIONAL HEALTH AND WELFARE, OTTAWA

[*The interim statement printed below will help to dispel current uncertainty on the status of the polio vaccine campaign. We await with great interest the final assessment of the situation when all the figures are in.*—ED.]

At this time it would seem appropriate to make an interim report to members of the medical profession on the situation with regard to poliomyelitis vaccine and to touch upon the present status and indications relating to its continuing use. In a manner of speaking, there is a lull in activities associated with the use of the vaccine, the first phase of the immunization programme having been concluded and now being assessed, and the second not yet commenced.

To review briefly the steps leading up to the present, it will be recalled that under the combined federal-provincial immunization programme, sufficient vaccine was prepared during last winter and through the spring of 1955 to permit the inoculation of somewhat under one million children in the age groups 5 to 8 years. By far the majority of these received at least two injections of the vaccine in accordance with Salk's latest recommendations. These programmes were carried on in all provinces commencing around April 12, the time of the announcement of the results of the 1954 field trials in the United States. Supplies of the vaccine were prorated amongst the ten Provincial Health Departments and were administered in accordance with their own plans, but generally to protect the age groups of children with the highest incidence of poliomyelitis.

All provincial programmes were concluded by or shortly after the end of June 1955 and it was deemed wise by provincial health authorities to suspend inoculations until the end of the "polio season".

Fortunately, this past summer was one in which the incidence of poliomyelitis was relatively low, on the basis of currently available figures, the second lowest year in the past decade. Up to the end of the first week of October, just over 800 cases of all types of poliomyelitis had been reported with approximately 390 of these described as paralytic. The five-year average to this date, 1950-1954 inclusive, shows 3,157 cases of all types with 1,525 paralytic. Thus it will be apparent that the incidence this year is somewhere in the vicinity of 25% of the average incidence over the past five years and seemingly the peak of the polio season was passed early in September, though the possibility of a further flare-up cannot be disregarded.

By agreement with the provincial authorities, studies have been carried on comparing the incidence of polio among groups of vaccinated children with that among unvaccinated controls. Thus it is hoped that additional data will be forthcoming from the use of the vaccine this past summer to provide further evidence of its effectiveness. It has been agreed that the tabulation of cases this fall will continue until November 30, 1955, and at the present time no conclusions can be drawn. Unofficial tabulations to date show a favourable indication in isolated instances. Since the numbers of cases are extremely small, because of the low incidence of the disease, and there still remain some weeks for additional cases to be listed and verification of existing and future diagnoses to be made, at the present time the situation might best be summed up by the generalization that the outlook appears favourable.

## REVERSIBILITY OF INDUCED PSYCHOSIS

Studies are reported of physicians given LSD-25 (lysergic acid diethylamide) in order to induce signs and symptoms suggestive of a psychosis. In 10 instances the psychotic effects of the drug were interrupted by intramuscular injection of 25 mg. chlorpromazine two hours after ingestion of the LSD-25. Chlorpromazine proved a rapid and effective antidote in reversing the signs and symptoms as well as the slight EEG changes which had taken place.—*Proc. Staff Meet., Mayo Clin.*, 30: 407, 1955.

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# PUBLIC RELATIONS FORUM

*Conducted by* L. W. HOLMES,
Assistant Secretary, C.M.A.

## V. TELEPHONE TACTICS

THE TELEPHONE as an emissary of good will and good public relations cannot be overlooked. Properly used, it can be one of the best friends a doctor has; abused, it can cause trouble.

When talking face to face with a person, one's words are coloured by facial expression. The speaker on the telephone is a disembodied voice, and the same words, lacking the support of a smile or a look of interest, may carry an entirely different meaning. Telephone tactics, therefore, can affect doctor-patient relations for better or for worse. Carelessly answered questions and carelessly worded conversations over the telephone, coupled with an inappropriate tone of voice, lead, perhaps more than any other factor, to misunderstanding of intent and purpose.

There are several basic rules which should be followed by anyone using the telephone:

1. Speak in a low, pleasant voice.
2. Speak slowly and distinctly.
3. Speak with authority, but not with brusqueness.
4. Speak in a normal tone of voice; don't shout, don't mumble.
5. Speak directly into the transmitter; lips should be about a half-inch from the mouthpiece.
6. Convey the impression that you are anxious to be of service.
7. Hang up gently. Slamming down the receiver is a discourtesy.
8. If you must leave the telephone to get information, suggest that you call the other party back.

Telephone courtesy should be stressed in the doctor's office. The telephone welcome should be as warm as the personal welcome. Cheerfulness, interest and friendliness should be reflected in the voice. The fact that the doctor or his assistant is hurried should not be conveyed by the speaker's voice or manner.

A patient calling the physician, in most cases, is surrounded with fear and worry because some member of the family is ill. From symptoms described, the doctor can frequently diagnose a condition as nothing serious and one that can await attention. But the anxious relative often does not understand this. Although the doctor may be busy, behind schedule, in a hurry, socially engaged, sleepy or annoyed, he must sound reassuring and interested on the telephone. The call should not be brushed off lightly.

If an emergency call should come in during the doctor's absence from the office or home, his receptionist or a member of his family should obtain this information: who is calling, address, nature of emergency, how the patient can be reached, patient's condition, the telephone number of caller. It is essential in gathering these facts that the person answering the telephone take sufficient time to get them accurately. This information should then be passed on to the doctor, who should always be within reach by telephone from his office or home.

Should the call not be urgent and the doctor feel that he cannot make the house call immediately, he can win friends by telephoning the patient to explain the fact, and to indicate when he might arrive. He should plan to arrive on time, or make another call to explain the second delay. This little courtesy will do much to set the patient's mind at ease and show that he has not been forgotten.

Many times a patient calls at the doctor's office for treatment of a minor condition and does not return. As time elapses, the patient is left wondering: "How does the doctor know whether or not I recovered?"

It is a sound practice for the doctor or his assistant to make a follow-up call inquiring about the condition of such patients. Or, as the patient leaves his office, the doctor may say: "Just call me in a day or two and let me know how you feel," or "Please be sure to let me know if you don't feel better." Such calls show that the doctor is sincerely interested in the patient. At the same time it cuts down on unnecessary visits.

Every doctor should have an understanding with his assistant about telephone interruptions. If possible, the assistant should find out whether or not the call is an emergency; if not, the doctor can return the call at his convenience. He must, however, remember to return the call!

One of the major complaints against the physician comes from poor telephone manners on the part of his employees. Every physician should, therefore, insist that courtesy and understanding be exercised by his staff in answering the telephone.

In summary:

1. Each physician should keep a close check on the telephone manners of his employees and his family. He should, moreover, set the good example himself.
2. Office employees should be carefully schooled in telephone habits. Local telephone company offices usually can provide free literature and films for this purpose.
3. The doctor should make it clear to his office staff and family that he wants to be informed promptly and fully on every telephone call regarding one of his patients.
4. The doctor should always let his office staff or his family know where he may be located.
5. The doctor should establish the habit of returning calls to patients.

6. If the doctor is going to be delayed in making a house call, he should call the patient and say so, specifying when he may be expected. A second call should explain further delays.

7. Telephone calls should never be treated lightly; more consideration should be shown over the telephone than in person-to-person contacts.

8. The doctor should participate in and let his patient know about emergency telephone call systems operating in the community.

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# GENERAL PRACTICE

## THE NEW BRUNSWICK CHAPTER

THE ANNUAL MEETING of this Chapter of the College of General Practice was held in the Algonquin Hotel, St. Andrews, on September 1, 1955, Dr. Melville Rice presiding.

Dr. C. L. Gass, President-Elect of the College, reviewed its activities of the past year. He stressed the importance of the "survey of general practice", an undertaking guided by a nucleus steering committee and having at its disposal $10,000 from the Canadian Life Insurance Officers Association. The purpose of the survey is to obtain a picture of the type and level of general practice in various parts of Canada, with a view to making recommendations for improving training for general practice and making it easier for general physicians to give high-quality service. When the survey is under way the co-operation of the Chapters will be necessary. Not every doctor will be interviewed or studied, but there will be a sampling of family doctors in various areas.

Dr. Gass felt that the members of the College should be interested in both reading and contributing to the special section of the *Canadian Medical Association Journal* reserved for general practice.

There was considerable discussion on the purposes of the Wyeth Postgraduate Education Fund and its significance for the Chapter in New Brunswick. It was stressed that all general practitioners would be welcomed at any extramural lectures organized by the College. The possibility of bedside clinics was discussed. It is not clear how popular these would be, but it is hoped that the replies to the recent questionnaires on education will give this answer. The Committee on Education would gladly receive suggestions regarding educational programmes.

A special committee to study the proposed by-laws of the College had been established at a meeting in Fredericton in August. This committee now proposed several changes in these by-laws.

The chairman asked for direction about the annual meeting of next year. One suggestion was that it be held on the first evening of the New Brunswick Medical Association Convention. Another suggestion was that it be held in conjunction with the Spring Clinical Sessions in Saint John, when a special day could be set aside for it. The decision was left with the executive.

*Officers for the year 1955-56:*

Chairman: Dr. Melville Rice, Campbellton.

Secretary: Dr. F. Emery Leger, Moncton.

Treasurer: Dr. S. D. Clarke, Lancaster.

Representative to the Board: Dr. Melville Rice.

Corresponding Member: Dr. G. C. Leger, Moncton.

Committee on Education: Dr. H. R. Bryant, Sussex; Dr. R. P. Myers, Moncton; Dr. J. L. Giovannetti, Newcastle; Dr. H. P. Melanson, Moncton; Dr. H. L. McKeen, Moncton.

The Committee on Education will assess the various postgraduate education programmes. To ensure uniformity across the country they will submit their rulings to the central committee for approval. They will also give consideration to the procurement of audio-aids, which reproduce transcribed lectures, for use in various sections of the province.

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## MEDICAL MOTION PICTURES

A COMMITTEE of the American Medical Association at 535 North Dearborn Street, Chicago 10, Ill., was organized in 1946 to promote a widespread and more intelligent use of medical films. It also acts as a clearing house for information on medical films. A library containing 106 medical films not readily available elsewhere is maintained. Some films suitable for lay audiences may be secured from the Committee. Reviews of medical motion pictures, screened by specialists, appear regularly in *J.A.M.A.* A booklet containing more than 500 reviews has been reprinted by the Committee. Sixty cents mailed to the A.M.A. Order Department will procure a copy.

A source list telling where and how to get most existing movies on medical subjects is also kept as a service to physicians and medical societies.

The *Bulletin of the American College of Surgeons* of September-October 1955 lists all films approved by the College and placed in

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their library. Reprints of "medical motion pictures approved by the College in 1955" are available on request to the Committee on Medical Motion Pictures, American College of Surgeons, 40 East Erie Street, Chicago 11, Ill.

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## TAPE RECORDINGS OF MEDICAL LECTURES

TWO YEARS AGO the Audio Digest Foundation was taken over by the California Medical Association. It had been founded a few months earlier as a private enterprise. It is now operated as a non-profit corporation and its surplus earnings are given to the 79 medical schools scattered across the United States.

As its name suggests, the function of the Audio Digest Foundation is to summarize and record on tape, current medical literature and lectures. In doing this, it checks some 1,200 medical journals each month, boils down the articles, and records the summaries. The Foundation states that the private doctor gets the equivalent of two hours of reading by one hour of listening to the tape. To give this service, a staff of 16 people read journals, and the selected material is then prepared by a board of editors.

The articles are sorted into five different categories—those that would interest the general practitioner, the surgeon, the pædiatrician, the internal medical specialist and the obstetrician-gynæcologist. Thus, five separate Digests are now being produced. The General Practitioner Digest is issued weekly. The other four Digests are issued twice a month. Each tape-recorded review of an hour's length is made up of a summary of 20 to 30 articles from the current medical literature, plus 15 minutes of lecture material by some outstanding speaker on a special subject.

The Audio Digest Tape Recordings have become a significant medium of postgraduate education for doctors. It now has nearly 3,000 subscribers. Some of them listen to it while travelling or making house calls and speak of it as a painless way of keeping up-to-date. The selection of the material presented is highly commendable. The extent of the service is shown by the fact that the subject index of the General Practitioner Digest for the last half of the year 1954 required seven pages for listing. Some State Chapters of the American Academy of General Practice give informal credits for Audio-Digest General Practice and apply it to a member's postgraduate education requirements.

The cost of these Digests is $2.75 each. A year's series of 52 Digests costs $143. A three-month trial series of 13 Digests costs $3.25 each—that is, $42.25 for the series. The tapes require machines to play them on. The following is a partial list of tape-recording machines suitable for using the Audio Digest Foundation tapes or those from any other country: Webster-Chicago (Webcor); Webster, Racine, Wisconsin (Ekotape); Revere; Pentron; R.C.A.; Wilcox-Gay; Sound Mirror.

No tape-recording machines have been manufactured in Canada, though we understand that one manufacturer has started to do so. These machines vary in price from approximately $200 to $300. The address of the Audio Digest Foundation is 800 North Glendale Avenue, Glendale 6, California. Information in Canada may be obtained from Dictating Equipment Ltd., 2434 Yonge Street, Toronto, or from your local dealer.

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## SURVEY OF CANADIAN GENERAL PRACTICE

IN THE FIRM BELIEF that a good family doctor service is essential to medical care, and that the first step in framing suggestions for helping the family physician is to study the present state of general practice, the College of General Practice of Canada in conjunction with the Department of Preventive Medicine of the Faculty of Medicine of the University of Toronto is arranging for a critical and analytical study of Canadian general practice. This will include study of the type and volume of illness treated by general physicians, the methods of treatment used, methods of office management, suitability of the present curriculum as preparation for general practice and other aspects of medical care.

This study is expected to take three years and the College of General Practice (*cf.* advertisement on page 35 of this issue) is anxious to hear from well-trained and competent physicians who would be interested in the post of director of the Survey, a post with a very promising future.

The director will visit selected practices for a few days at a time, and sit in with the doctor during office consultations and home and hospital visits, first in a pilot series in Ontario and later in a series drawn from a number of provinces of Canada. A full and detailed account of this project will appear in the December 1 issue.

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# MEDICO-LEGAL

## DEATH FROM LOCAL ANÆSTHETIC

### SETTLEMENT REFUSED

T. L. FISHER,* M.D., *Ottawa.*

IN MAY 1953, a urologist, a man of experience with an exceptionally good record in practice, advised a young married woman that cystoscopic examination should be done. Three years previously he had cystoscoped her under local anæsthesia without any unfavourable reaction. For this cystoscopy the same preoperative preparation was given and the same local anæsthetic was ordered—three ounces of Nupercaine 1 in 500. It was routine in his hospital for the local anæsthetic for female patients to be instilled through a catheter by a nurse on the ward some 15 minutes before patients went to the operating room, and the routine was followed in this case. The urologist entered the cystoscopy room on time, and found his patient nauseated and vomiting a small amount. For a few minutes she conversed freely with him and then ceased to pay any attention. Pulse and respiration were normal but she seemed to be losing consciousness. Oxygen by inhalation was begun immediately and the chief anæsthetist of the hospital came quickly and gave emergency treatment but, in spite of this, respiration became laboured and two short convulsions occurred. Her condition gradually worsened, and she died an hour and a half after she reached the operating room.

At the inquest two toxicologists from the Provincial Laboratory testified that the solution of Nupercaine used was between 2.8 and 3.4 times as strong as that ordered by the urologist. Their impression was that the patient died from Nupercaine poisoning. The verdict of the coroner's inquest was that the patient came to her death as a result of the use of a solution stronger than that prescribed by the attending physician.

In February 1954 a writ was served on the urologist, as one of several defendants, claiming $20,250. Consultations with the urologist and the solicitor for the Canadian Medical Protective Association made it seem clear that the urologist's orders had been correct and proper, that his experience with the patient gave him every reason to believe that the anæsthetic chosen was a suitable anæsthetic for the patient and, therefore, that he was in no way to blame for the woman's death. Though the doctor could have avoided the strain, the worry and the work of preparing to defend himself—and these were particularly burdensome for him because of a recent illness—he accepted the Association's advice that he should not consider settlement at all.

The case actually reached court but, before trial had progressed beyond the preliminaries, was settled by one of the other defendants and dismissed against the doctor.

Much that is interesting about the case is robbed of value because, there having been no trial, no facts were established, but there is one point of importance to the medical profession which is well illustrated by this case. A doctor is wise who, when faced with a claim for a poor result that was not his fault or may even have occurred in spite of him, decides to defend himself vigorously. In this case a small contribution from the doctor as his part of a larger settlement by the other defendants would have settled the claim against him. The temptation to accept it was great. As far as anyone could tell at that time, if he refused to make the small settlement the surgeon would have to stand trial, with all the worry and work and publicity this would mean. The fact that, in the event, his refusal to make any financial settlement was followed by collapse of the action against him rather than by trial, does not detract from the credit he deserves for his pluck and wisdom.

It is folly for the individual doctor, and a disservice to his confrères, to accede to unjustified demands in the hope that thereby he will be spared trouble. Such settlements are not kept secret. They are a matter of public record. Every dissatisfied patient is a little more encouraged if he is tempted to seek a financial settlement. Claims of this kind settled unnecessarily breed more and bigger claims against more and more doctors. Every one makes the practice of medicine more hazardous, particularly for those doctors in the district where a settlement is made, and distracts doctors from their medical work because they must give some thought to their own protection in case of unjust claims against them instead of single-mindedly doing the best work possible for their patients.

When faced with claims doctors should have two things clearly in their minds. The first is that unnecessary settlements harm themselves and increase the legal hazards of practice for all doctors. The second is that courts of justice are courts of justice; they can be relied on for protection when doctors are right. Therefore, when charged unjustly, doctors should not become hesitant and overcome with fear but should defend themselves as vigorously as possible. That way they help themselves and their confrères.

*Secretary-Treasurer, Canadian Medical Protective Association.

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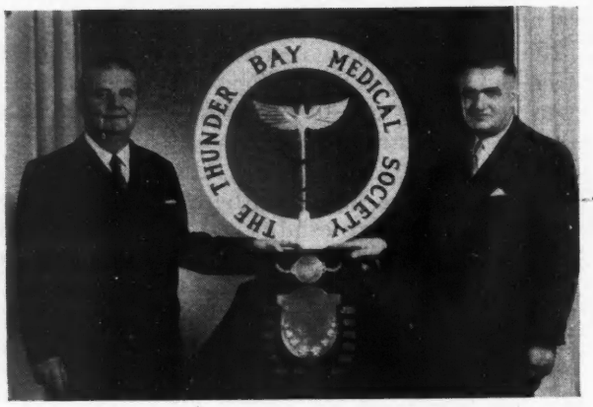
# MEDICAL SOCIETIES

## THUNDER BAY MEDICAL SOCIETY




Winner of the T. C. Routley Shield every year since 1953, the Thunder Bay Medical Society proudly exhibits the proficiency award at the Lakehead Summer School, September 15-17, and annual meeting of the Ontario Medical Association, District 10. Seen above, left to right, are Dr. R. K. Dewar, F.R.F.P.S., and Dr. N. A. Ost, A.I.C.S., F.I.M.A. with the award presented at the B.M.A.-C.M.A.-O.M.A. Annual Meeting in Toronto in June. The Thunder Bay Medical Society topped 51 other societies in general proficiency and postgraduate work to win.

# MISCELLANY

## TRAFFIC IN NARCOTIC DRUGS

The Proceedings of the Special Committee of the Senate appointed to enquire into and report upon the traffic of narcotic drugs in Canada and related problems has been published. It will be recalled that a committee of 23 senators, with the Honourable Tom Reid as chairman, held public hearings this year in Ottawa, Vancouver, Toronto and Montreal, in addition to a number of other sittings.

Their report is divided into two sections. The first is a general statement of the position and the second contains conclusions and recommendations. The Committee reviewed Canadian legislation dealing with narcotic drugs and records its favourable impression of the efficiency with which the Opium and Narcotic Drug Act is administered by the Division of Narcotic Control of the Department of National Health and Welfare, headed by Mr. K. C. Hossick. The Committee also comments that Canada, as a member of the United Nations, has agreed to prohibit the legal importation of heroin. As regards drug traffic, the Committee considers that there is an illicit drug traffic in Canada with about one half centered in British Columbia. Figures indicate that at the present time there are in Canada a total of just over 3,000 addicts, classified as 515 medical addicts, 333 professional addicts and 2,364 criminal addicts. There is, however, no juvenile or teen-age addiction problem in Canada.

Heroin is the most commonly employed drug of addiction, marihuana apparently being uncommon. Evidence as to treatment leads the Committee to conclude that the establishment of narcotic clinics or the provision of any other legalized supply of drugs for the purpose merely of supporting addiction would be a retrograde step. Educational programmes may usefully be established for adult groups generally, but should not be so used as to arouse undue curiosity on the part of impressionable persons or those of tender years. The Committee recommends improvement and expansion of mental health programmes in schools in the hope that variations from acceptable behaviour may be detected and treated before the opportunity for drug addiction arises. It was so impressed with the high quality of narcotic drug research in Canada that it comments that Canada may become a drug research centre for foreign students.

### CONCLUSIONS AND RECOMMENDATIONS

Evidence of medical authorities indicates to the Committee that drug addiction is not a disease in itself, but a symptom of character or personality defect. Because of this, relatively few cases have been reported of drug addicts who, while out of custody, have succeeded in abstaining from the use of drugs for any lengthy period.

The Committee reviewed the responsibilities of the Federal Government, whose work it is to suppress illicit distribution and use of drugs, and of provincial authorities who are responsible for treatment of drug addiction. The drug addict population engages in crime at frequent intervals in order to obtain supplies of drugs, and therefore requires for its control vigorous police and community action. The provision of facilities for treatment by provinces (British Columbia has none at present) is an urgent matter. By using its constitutional power, any province could pass the necessary legislation for committal of drug addicts to an appropriate treatment institution, either on a compulsory or a voluntary basis. If the problem is too large, an effort should at least be made to treat the young ones. The need for follow-up of addicts who have been treated is also stressed.

The Committee consider that the penalties for trafficking regardless of whether the trafficker is or is not an addict should be made more severe. It also recommends that association of an addict with a juvenile should be considered prima facie evidence of contributing to delinquency.

## PARABLE OF THE HEALERS

*[Inspired by recent discussions between Mr. Frost and Mr. St. Laurent on National Health Insurance.]*

Now in a certain country there was a great guild of healers because this type of art appealed mightily to all the people. And it was said by some that this was the strongest union in the land. And it was a hard thing to enter the guild, for only the learned could apply and they worked the first eight years without pay, even as apprentices, and those who aspired to be master craftsmen worked a further five years for a pittance. Then, if their work found favour, they could labour as many hours as their strength allowed. And those whose names became noised abroad did make substantial contribution to the tax gatherer. But because of the tax laws and the style of living expected of their prestige as artists, none of their estates were talked about in the market place.

Now it came to pass that certain politicians spoke to the people saying "Why should each man have to pay for his healing—let the state control the healers." And because many people hope for something for nothing, a law was passed. But behold, the matter turned out ill. For the healers, a proud guild, waxed exceeding wroth. "Have we not for many years worked for the poor for nought?", they said. "And does not the guild ensure sufficient treatment to all for a small monthly fee? And must we now be ground under the feet of servants of the state who know not our ways and are full of the

insolence of office and the law's delays, and swollen with our substance?"

And the strongest and best of the healers shook the dust of that country from their feet and departed thence. And those who were left said to themselves "If we are to work for the state with no reward for merit, we will work in the manner, and at the pace, and for the hours, of other servants of the state, and by Æsculapius we shall take our ease that our days may be longer in the land." And indeed the excellence of the work declined from that hour, but the parchments multiplied.

And the sons of the healers sought other work.

F. G. ALLISON

# CORRESPONDENCE

## ETHICS, THE DOCTOR AND THE SOCIAL SCIENTIST

*To the Editor:*

A most worthwhile point has been presented in the article, "Mothers, Mongols and Mores", regarding the separation of defective children from their parents. The authors are of the opinion that a physician as such must not make ethical decisions for his patient, although the same physician, as a citizen, may attempt to alter the mores of society. The separation of defective children is a social and moral problem, and if the physician is "prudent he will try to determine the unintended and unexpected consequences of such changes before advocating them". Such foresight is no doubt the essence of prudence, but it does not follow that to do this "he must have recourse to the social scientists for help", as though this were his only hope of achieving the enviable virtue. No doubt these scientists may help, but let us not fall into the same trap from which we would save our patients, the humble obedience and quasi-deification of those to whom we attribute scientific knowledge and ability. For is not the social scientist, engaged in the difficult task of digging the foundations for his discipline, subject to the same prejudices, confused loyalties and scotomata of the average citizen? Is he any more able to cope with these problems at the present time by reason of having the crude scientific tools now at his disposal and his greater collection of data? In short, may not the "terms of reference" of such ethical problems be too broad for the social scientist? Steam engines did not run for a long time after the tea kettle was invented.

The social scientist is not only groping at the present stage, but is often intimidated by the pressure to conform. Which social scientists have spoken out on the much graver ethical issues of the atomic and hydrogen bombs? Unfortunately they too often hide behind the excuses that such problems are not in their field, or that there are insufficient data. The social scientist, too, has to make decisions as a citizen, such as the decision to conform, and these will influence the direction and outcome of his research.

I do not wish it implied that I am not in favour of the social scientist having a go at the problem of the mental defective raised by the authors. I merely wish to avoid a naïve faith that we must rely on them. It has been said that no country is safe in the hands of its experts. Adequate decisions and changes are often made by the non-scientific general public, when the necessary information is placed before them.

Calgary, Alta., F. W. HANLEY, B.A., M.D.
October 7, 1955.

## HILTON'S "REST AND PAIN"

*To the Editor:*

In 1950, G. Bell and Sons published John Hilton's book, "Rest and Pain", edited by Walls and Philipp. Five editions were published under this title, and in the introduction to the new volume Mr. Hedley Atkins credits Jacobson with the last four. The last edition was in 1892, and there were 10 reprints, the latest being in 1930. Jacobson's notes, indicating contemporary thought, made up the bulk of the book. These had to be read against the background of the last decade of the 19th century, whereas the lectures were delivered 30 years earlier; as the form of the book was not modern, it did not make easy reading.

The new volume is attractively bound and printed, with illustrations and photographs, and a short biography of Hilton. There is a minimum of alteration, and the comment is reserved until the ends of the lectures. In an appendix, there are short biographical notes on some of Hilton's contemporaries.

Dr. Gibson regards Hilton's views on anatomy as teleological, and this may well be so. We must think of Hilton in relation to his time, and his style as that of a hundred years ago, and that conventional modes of expression frequently need interpretation. These were lectures and not essays, and Hilton apologizes on this score for their "tautology and colloquial and unstudied style". A lecturer is afforded a licence which is not allowed an author, and that which sounds well frequently reads badly. Of his ability as a lecturer there is no doubt, and Addison, who was several years his senior, made a point of attending his lectures on the central nervous system. He had a dynamic approach, which put the flesh on the dry bones of the anatomy room and made them live, thus imparting knowledge and stimulating interest, if we are to accept the extract given in the introduction as a fair sample of his lectures. The subject is the vomer, a source of confusion to most medical students, and probably forgotten by all except the ultra-specialists. Hilton makes it the keystone to the architecture of the face, and the link between the face and the base of the skull, using all the skill of a master to make it easily understood and remembered. Students must have appreciated such lectures. All doctors must have had to listen to lectures which were models of exactness, both as to the subject matter and the choice of words, and nearly all must have been bored and become disinterested. His style is well worth study for directness, concise phraseology, and the avoidance of the eponym.

The content of the lectures may not withstand critical examination today, but we may well pause to think what it represents. Hilton lived at the end of an era. Anæsthesia had arrived, but Hilton had probably matured professionally before this. He had had the honour of performing the autopsy on Sir Astley Cooper, and in Guy's he had Bright, Addison and Hodgkin among his contemporaries. These lectures given to the recently formed Royal College of Surgeons probably represented the best in surgery at the time, with a review of recent work and comment on controversial topics. Soon after this, the face of surgery changed, and has been changing constantly ever since. so that something that was new is forgotten in 10 years, and there is little agreement on any problem, either from time to time in the same place, or at different places at the same time. Such a simple problem as whether the patient should get out of bed immediately after an operation or not provokes a long and inconclusive argument. The interpretation of results is probably the most difficult problem of all, and as this represents the social usefulness of surgery, we can be accused of losing our perspective. Hilton gives an impression of thought and practice before this change took place. Here is a philosophical approach to the problems and limitations of surgery of a hundred years ago, well edited and eminently readable.

P. W. HOPPER, M.D.

The Winnipeg General Hospital,
Winnipeg, Man., Oct. 16, 1955.

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# OBITUARIES

DR. J. A. C. ETHIER died in Sherbrooke on October 5 at the age of 82. After graduating at the University of Montreal, he practised in Valcourt for nine years before moving to Sherbrooke where he was in practice for 49 years. During this time Dr. Ethier specialized in urology. For many years he was the director of the original Hôtel-Dieu Hospital in Sherbrooke, of which he was one of the founders. In 1949 the Order of Knight of St. Gregory the Great was conferred upon him by Pope Pius XII.

Three times a widower, Dr. Ethier is survived by four sons and four daughters.

DR. ROBERT BUCHAN FRANCIS, a practising physician in Calgary since 1909, died in the General Hospital, Calgary, on September 30 at the age of 74.

He was born in Mitchell, Ont., and went west to Ft. Macleod, Alta., to work for a year before returning east to complete his education. He received his medical degree from the University of Toronto in 1908. Dr. Francis was an honorary member of the Calgary General Hospital staff.

He is survived by two sons, Dr. Robert R. Francis, Edmonton, and James R. Francis, Calgary, and a daughter.

DR. HENRY FUNK, head of the department of orthopædic surgery at St. Boniface Hospital, died on October 19, aged 50. Born in Altona, Man., he took his B.A. at Wesley College, and his medical degree at the University of Manitoba. Later he became a member of the Canadian Orthopædic Association, a Fellow of the Royal College of Physicians and Surgeons of Canada, and a member of the teaching staff of the medical faculty of Manitoba University and of the attending staff of St. Boniface Hospital. He was consultant in orthopædics to the Manitoba Sanatorium.

He is survived by his widow and three daughters.

DR. WILLIAM HARRIS, 60, died of a heart attack at his home on October 10. In practice in Toronto for 37 years, he was the only general practitioner appointed as consultant to the New Mount Sinai Hospital.

Born in Grand Rapids, Mich., Dr. Harris had lived in Toronto since his boyhood. He received his medical degree from the University of Toronto in 1918, served as captain in the Canadian Army Medical Corps during the First World War, and set up practice in Toronto upon his return to civilian life.

His eldest son having been killed in action on D-Day in Normandy, Dr. Harris is survived by two other sons and his widow.

DR. MARCUS LORNE JEWETT of Millville, N.B., died on October 8 in the Victoria Public Hospital, Fredericton. Dr. Jewett was born at Keswick Ridge, N.B., in 1888 and received his education at Keswick Ridge Superior School, the Provincial Normal School, and McGill University. His graduation in medicine in 1914 was followed immediately by the establishment of a practice at Millville which he continued until recently when ill health overtook this busy rural physician. Dr. Jewett served as a member of the Provincial Legislature from 1930 to 1935. He had been recently appointed Honorary President of the York County Progressive Conservative Association.

Dr. Jewett was a good friend, and that sums up his position in his community, his political party and in the practice of medicine. He scorned pretence, was straightforward and unassuming, proud of his family and of his friends—lay and professional. His professional life was guided by his sound principles and his attendance at medical meetings and conventions renewed his friendship and professional knowledge. Many persons in New Brunswick will long remember this kindly, humble doctor.

He is survived by his widow; one son, Dr. Beverly L. Jewett; and one daughter, Geraldine.

DR. DANIEL PAUL KAPPELE of Hamilton, distinguished soldier and well-known doctor, died at Hamilton General Hospital on September 28. Dr. Kappele was a native of Hamilton. After graduating from the University of Toronto in 1903, he interned at Hamilton General Hospital and later trained at Johns Hopkins Hospital in Baltimore.

Lieutenant-Colonel Kappele was one of the first commissioned officers with the Fifth Field Ambulance C.E.F. in 1914, and was awarded the Distinguished Service Order and Bar for his services in the First World War. Upon returning to Canada, he was put in charge of the Brant Military Hospital at Burlington. He was President of the Hamilton Academy of Medicine in 1922 and became a staff member of the Hamilton Board of Health. During the Second World War he served as president of the medical board in Hamiilton.

He is survived by his widow and a son and daughter.

DR. WARREN SOPER LYMAN, 79, a specialist in internal medicine, died suddenly at his home in Ottawa on September 25. For more than half a century he had practised his specialty in that city.

Dr. Lyman, who was born in Dubuque, Iowa, attended McGill University, after graduating with the degree of Bachelor of Philosophy from Grinnell College, Iowa. In 1904, a year after obtaining his medical degree from McGill University, he went to Ottawa as a resident physician with the County of Carleton General Protestant Hospital. He was with the Montreal General Hospital as resident physician from 1906 to 1907 and was resident pathologist and bacteriologist during 1907 and 1908. In the latter year he returned to Ottawa to open private practice. From 1909 to 1918 he was pathologist for the County of Carleton General Protestant Hospital and from 1912 to 1925 was physician there. He had been associated with the Ottawa Civic Hospital since 1925, serving as chief of medical service from 1934. He also acted as consulting physician to Strathcona Hospital from 1937 until his retirement from that post several years ago.

Dr. Lyman was a charter Fellow of the Royal College of Physicians of Canada in 1931, and of the Royal College of Surgeons of Canada since 1933. He served the combined bodies as honorary secretary from 1932 to 1944.

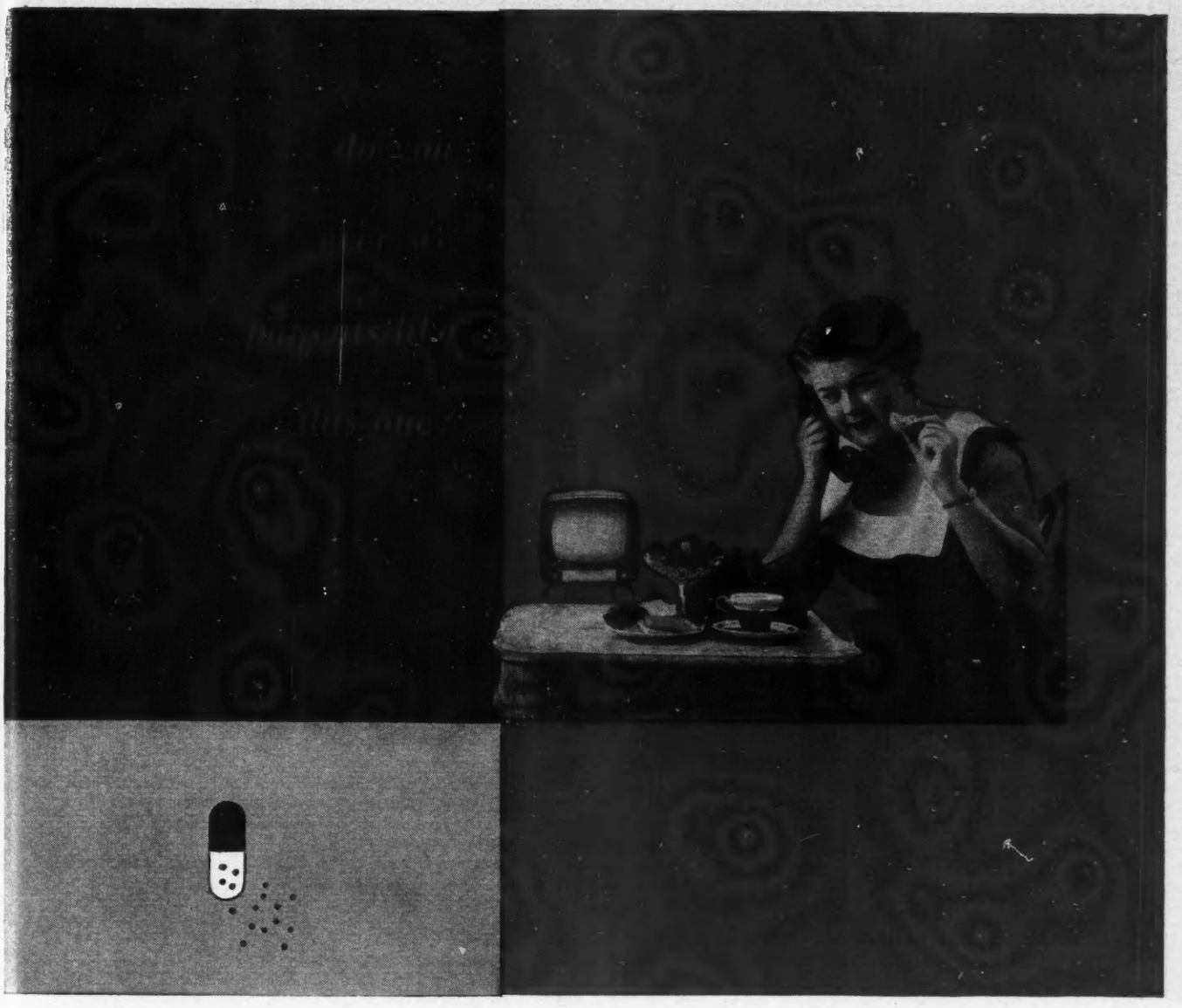
He is survived by his widow.

DR. ADEN FLOYD MACINTOSH of Andover, N.B., died at his home on October 5 after a year's illness. He was born in Dundela, Ont., in 1885 and received his early schooling there. Before entering McGill Medical College he was a schoolteacher for several years. After graduating in medicine he settled in Andover in 1914 and had practised there for 40 years. Like many busy doctors he also served his town in many civic interests, especially as a school trustee.

Dr. MacIntosh took an active interest in the Masonic Order and was an ardent horseman both as an owner and promoter of organized racing. He was also interested in the Saint Andrew's Society and was the first president of the Upper Saint John River Branch. The members of the Society, headed by Pipe Major Downie, led the funeral procession, and following committal, the Scottish lament "Flowers of the Forest" was played by the piper at the graveside.

Friends and patients from the Andover area and many points throughout the province attended the services at the late doctor's home and the Baptist church.

Dr. MacIntosh leaves his widow, three sons and three daughters. One son, Dr. Robert A. MacIntosh, practises in Fredericton.



Grace has two grown children who now live in other cities. After years of intense activity, she is left with little to do and think about. Her days are spent with the television set and telephone, and she is usually nibbling. Her weight increases slowly, but steadily.

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# BOOK REVIEWS

## NEUROPHARMACOLOGY

*Transactions of the First Conference, May 26-28, 1954. Editor, H. A. Abramson, Assistant Clinical Professor of Physiology, Columbia University College of Physicians and Surgeons, New York, N.Y. 210 pp. Illust. $4.25. The Josiah Macy, Jr. Foundation, New York, N.Y., 1955.*

The Conference programme of the Josiah Macy Foundation has performed a unique service for investigators and advanced students in biology and medicine. These discussions are conducted and published in an effort to stimulate research and to promote effective communication across the physical and verbal barriers which tend to isolate various disciplines and specialties. Discussion is organized around a particular field which is undergoing intense current investigation. The participants are selected for their interest in the chosen field and for the diversity of their viewpoints. While the programme is organized around a number of prepared presentations of the results of current research, an informal atmosphere conducive to the free exchange of ideas is consistently maintained. About 20 such groups have been organized during the past decade, each meeting annually over a period of three to five years.

The current volume is the first in a new series entitled "Neuropharmacology". This field has recently received a considerable impetus from the introduction of a wide variety of new agents, with more discrete psychological effects than those hitherto available. The vigour and scope of the discussions in the present volume fully measure up to the high standards established by previous Conference groups.

The programme opens with a consideration of the circulation and energy metabolism (oxygen consumption) of the brain and the effect of drugs thereon. The subject is succinctly and critically reviewed by Dr. Seymour Kety, whose techniques and original investigations have contributed so extensively to the development of this field on a firmly quantitative basis. This is followed by Dr. Ernst A. Scharrer's fascinating account of the correlations which exist between the organization of the vascular pattern and other anatomical and chemical patterns of organization (cell inclusions, histochemically localized enzymes) in the brains of a variety of animals. The functional correlations of these spatial patterns remain obscure.

Attention is next turned to the EEG patterns associated with consciousness, sleep and sensory arousal, and the influence of anæsthesia and narcosis thereon. The introduction and general survey by Dr. Mary Brazier concludes with a most interesting discussion of the delayed (Forbes) response to sensory stimulation. This is followed by Dr. Horace W. Magoun's account of the ascending reticular system and its presumed relation to consciousness and arousal. This concept, which has aroused so much interest in recent years, is summarized in concise yet lucid fashion and the effects of central depressant drugs on this response are described. The symposium concludes with a discussion of some recently developed convulsant drugs by Dr. Carl C. Pfeiffer. These acridones possess fluorescent properties, and hence their localization within the central nervous system can be observed histologically in some detail. The possible correlation of localization to pharmacological action remains a matter of conjecture.

## ANNUAL REVIEW OF MEDICINE

*Volume 6, 1955. Editor, D. A. Rytand; Associate Editor, J. Anderson, Stanford University School of Medicine. 459 pp. $7.00 (U.S.A.), $7.50 (elsewhere). Annual Reviews, Inc., Stanford, California, 1955.*

The Annual Review of Medicine for 1955 contains 21 chapters on many aspects of medicine. It begins with one on the problem of keeping up with medical literature, and ends with an annotated list of over 500 reviews. It is more than a "recent advance" type of presentation. In the chapter on laboratory aids to diagnosis and treatment, the author not only reviews the recent literature but tells readers how to use it to the best advantage. He does the same thing for the clinical laboratory itself.

The reviewer for psychiatry emphasizes the newer pharmacological agents which are revolutionizing the treatment of psychiatric disorders. The neurologist discusses clinico-pathological studies in such conditions as the peripheral neuropathies.

Cardiovascular diseases are discussed from the surgical as well as the medical side. A few of the other contributions of special value because of their complete coverage are the chapters on viruses, nutrition, allergy and cancer.

Useful and significant contributions have been selected by all the reviewers. The important advances in each subject have been synthesized and presented in a manner that makes for easy reading and sustained interest. The volume is highly recommended for the reference library, the bedside table or for the weekend brief-case of physicians who enjoy medical scientific literature and strive to keep up with its progress.

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## THE JOINTS OF THE EXTREMITIES

*A Radiographic Study. Notes on Non-routine Methods, Non-routine Ideas, and Less-common Pathology. R. W. Lewis, formerly Director, Department of Radiology, Consultant in Roentgenology, The Hospital for Special Surgery, New York, N.Y. 108 pp. Illust. $9.50. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1955.*

This atlas type of book devotes its attention to non-routine x-ray procedures and less common pathology of the joints of the extremities, including hip and shoulder. Special attention is given to the analysis of the soft tissue shadows of the joints and an attempt has been made to describe radiological techniques involving the areas concerned, to be used when the patient is unable to co-operate freely. There is a definite need for an instructive manual on radiographic technique which limits its descriptions to the radiography of the injured part in those patients who are too ill to co-operate, in plaster, in traction or are affected with other forms of disability. This book partially fulfils this need.

The author has utilized large line drawings to demonstrate the alterations of contours of accompanying bone and soft tissue radiographs. The film reproductions are of good quality and generous in size. The chapter on "the shoulder" is the most comprehensive, describing periarticular soft tissue changes and various radiographic positions in some detail. Orthopædic surgeons, anatomists and radiologists will find the book interesting and instructive.

## DE ABDITIS NONNULLIS AC MIRANDIS MORBORUM ET SANATIONUM CAUSIS: THE HIDDEN CAUSES OF DISEASE

*Antonio Benivieni of Florence; translated by C. Singer. 217 pp. Illust. $7.50. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1954.*

This is a minor, but important, classic. It is a source book in the history of pathological anatomy, 250 years older than Morgagni's famous *Seats and Causes of Diseases*. Between 1507 and 1761, between Benivieni and Morgagni, autopsy records accumulated, many were published, and they came to play a greater part in medical theorizing and research. To say that all this was willed and started by Antonio Benivieni would be inexact. This able, well-educated Florentine physician kept notes of his more interesting clinical cases, some 160 in all, of which 111 were chosen for publication five years after his death; only about 15 necropsy protocols were included. Post-mortem examination in puzzling cases was far from uncommon in fifteenth-century Florence. "It was the orderly mind of Benivieni, as much as his professional capacity, that made him a pioneer in the sciences of pathology and nosography. The Benivieni who kept . . . careful records of his sales, exchanges and purchases, the rents from his properties and the contents of his library, was an equally faithful bookkeeper of his medical experience." The little work so produced was revolutionary neither in purpose nor in immediate effect, but it was nevertheless a seminal work, unmistakably influential.

If approached in a true historical spirit, this is still a rewarding book. It pictures humoralistic Renaissance medicine and surgery in an attractive way. It shows its author to have been learned, conscientious and sensible. It reveals the root and origin of modern pathology. If, however, the reader has in mind the somewhat otiose praise of Benivieni which has appeared in more than one history of medicine, and looks to find the work of a proper modern who lived "before his time", disappointment is certain. No more should one expect to find current ideas of political democracy enshrined in Magna Carta.

Dr. Singer's translation is accompanied by a facsimile of the original Latin edition, five handsome illustrations, and helpful but all too brief editorial notes. Dr. Long's biographical introduction is excellent.

## OFFICE PROCEDURES

*P. Williamson. 412 pp. Illust. $12.50. W. B. Saunders Company, Philadelphia, 1955.*

When a general practitioner writes a book on general practice, one expects something direct and straightforward. Dr. Williamson has written such a book in just this way. He picks out only the things which should be dealt with in office practice; for example, he says: "the treatment of extensive burns is completely out of the field of minor surgery". He goes on to qualify this in the case of children, in whom as he says even minor burns may require hospitalization. He also says that neglect of minor burns is the best possible treatment, although he allows that this is not generally accepted. But he does not dogmatize and this adds a great deal to the attraction of the book.

He can, however, be forthright; for example, "This pernicious test (the B.M.R.) is, in the hands of the average practitioner, an inaccurate nuisance."

The author has wisely depended a great deal on small line drawings to help in making his points, and these, along with his clear and attractive style, make up a volume which is well worth having.

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